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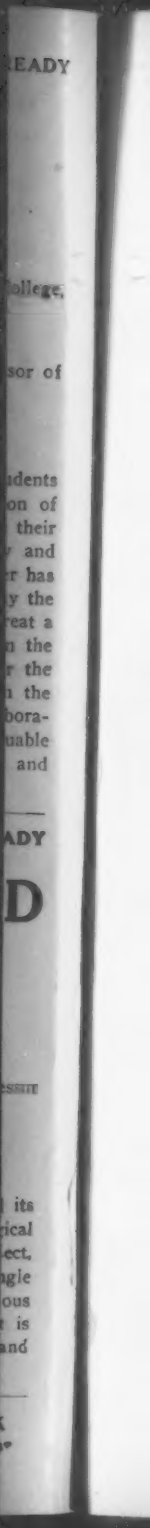

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

JUNE, 1912

ORIGINAL ARTICLES

SURGERY OF THE BILE DUCTS.[1]

By John B. Deaver, M.D., LL.D.,

PROFESSOR OF PRACTICE OF SURGERY, UNIVERSITY OF PENNSYLVANIA; SURGEON-IN-CHIEF, GERMAN HOSPITAL, PHILADELPHIA.

It can truly be said that our present knowledge of the pathology of the abdominal viscera, and particularly of those of the upper abdomen, is directly due to the development of modern abdominal surgery. And foremost among these structures whose diseased conditions have been made manifest by surgery we can consider the biliary system with its accessory organs, the gall-bladder and the bile ducts, and the pancreas.

I have dwelt many times upon the importance of living pathology, the direct examination of diseased processes *in vivo*, the opportunity for which has caused it to be truly said that the internist walks by faith, the surgeon by sight. The study of living pathology enables the surgeon, and the internist if he will avail himself of its opportunities, to distinguish fundamental conditions from end results. It enables us to attack pathological conditions in their incipiency and often to diagnosticate them at a time when treatment will still be of avail.

Surgery of the bile ducts, in association with the work of men in the laboratory, has demonstrated that with the exception of malignant disease all the conditions which call for surgical interference upon any part of the biliary tract have their origin in infection. Even malignant disease, though probably not itself of infectious origin, seems to bear some relation to antecedent infec-

[1] Read before the Medical Society of the State of New York, Albany, N. Y., April 17, 1912.

tious processes since it is found most often in organs which bear the traces of previous inflammation. The long train of biliary disease, with its complications and sequelæ, has therefore as its one exciting factor the harmful activity of pathogenic micro-organisms.

The infecting agent may reach the biliary tract in a number of ways, but it seems likely that it generally arrives by way of the portal circulation. There is no doubt, however, that microörganisms may enter the biliary tract directly from the duodenum, and this seems to be the case in those instances of cholecystitis and cholangitis directly consequent upon an intestinal catarrah.

Whatever the route of infection a number of organisms are concerned in the production of biliary disease, each one of which alone or in combination with others gives rise to many different pathological conditions.

As a general rule it may be accepted as proved that low grade infections by microörganisms greatly attenuated give rise to gall-stone disease, or cholecystic inflammation with the formation of stones, while acute invasions of the biliary tract by organisms of high virulence give rise to acute forms of cholecystitis, cholangitis, and their accompaniments too rapidly to permit of the formation of stones. Such acute infection again may partially subside and be converted into a sluggish stone-forming catarrh.

As has been mentioned, no one form of disease of the biliary tract can be identified with a particular organism. Thus, of 142 operations in 1911 on the biliary tract for various lesions, 34 showed bacillus coli, 50 showed no growth, in 46 the organism was not mentioned, 2 showed Bacillus typhosus, 7 Staphylococcus albus, 1 streptococcus, 1 Bacillus pyocyaneus, 1 Bacillus aërogenes. It is worthy of note that in many instances where infection was evident, that is, in the presence even of pus, cultures showed no growth. Either the organisms present were not such as could survive upon ordinary culture media, or that which seems more likely, the offending bacterium had died out while the products of its activity remained.

The preponderance of the colon bacillus is not remarkable. It is a well-known fact that this organism is at all times present in a large portion of the alimentary tract and that most infections of a portion of this tract soon become mixed in the presence of this widely distributed and hardy organism. The colon bacillus then overgrows the original invader and alone is found when the case comes to operation. This fact together with the ease with which this organism is cultivated and identified probably gives it a statistical importance somewhat beyond its actual deserts. There can be no doubt, however, that the colon bacillus may be the infecting organism at the outset and by itself may produce all the varied consequences of infection of the biliary system.

In other series the Bacillus typhosus has been found in a greater percentage of cases. Thus in 182 cases of cholelithiasis, reported by me in 1906, there were cultures made in 94, and of these, 13, or one-seventh, showed the presence of the typhoid bacillus. In one instance this organism persisted forty-one years after the original infection. We have found this organism in the gall-bladder in cases where the most careful inquiry failed to elicit anything like a previous attack of typhoid fever. I have known typhoid fever to immediately follow an operation for the removal of stone from the gall-bladder where cultures from both the gall-bladder and the interior of the stone removed showed the typhoid bacillus.

These figures are of interest in view of the possible role of the Bacillus typhosus in the causation of cholelithiasis. It has been found that a large proportion (in this series 22 per cent.) of gall-stone cases give a history of having had typhoid fever, and it seems in many of these as if we could directly trace the beginning of symptoms referable to the biliary system to a period not long after the typhoid infection. The typhoid bacillus has repeatedly been demonstrated in the centre of biliary calculi, and it is probable that it bears a closer relation to the origin of biliary disease than the study of cultures at the time of operation would indicate.

Each organism of the small series given, and others also, has been found capable of giving rise to the most diverse conditions within the biliary tract, and no special set of changes can be charged to any particular organism.

In contradistinction to the old view that most cases of gallstones are without symptoms, we know now that all of them have symptoms and most of them very evident ones. We have learned that infectious conditions giving rise to marked pathological changes in the right upper quadrant of the abdomen are not different from similar processes in any part of the body, and that they must and do make themselves known by symptoms needing only correct interpretation to make a diagnosis certain. As our diagnostic powers improve and surgical cure is more often sought, we shall meet with fewer and fewer instances of the extensive complications found in so many cases of this series, just as it is rare nowadays to find an instance of the huge ovarian cysts formerly so common and so spectacular from the operative standpoint.

Since infection is the underlying cause of biliary disease we must rely in this, as in other cases of infective disorders, upon that great surgical principle of the treatment of infection—drainage. And we have demonstrated that the biliary tract is no exception in yielding to the correct application of this principle. Every operation upon the biliary ducts must serve a double purpose, it must meet the immediate mechanical demands of the conditions found, and it must furnish drainage for a sufficient length of time to cure infection.

Could we get these patients in the early stages of the disease there would be nothing to meet but the infection—in other words, cholecystostomy would suffice; a simple operation quickly performed, and, with proper care in the selection of patients, almost without mortality. It is a high aim to get our cases in this stage, but it is not too high, and should command the united efforts of the profession. Unfortunately it is in just this stage that the disease is most difficult of diagnosis, the physician most reluctant to advise, and the patient to accept operation. The same educational campaign which has won such a signal victory in appendicitis must now be carried on in this field. All cases of indigestion should be most carefully scrutinized for the evidence of localization in the gall-bladder. Slight epigastric distress; occasional tenderness in the right hypochondrium, sometimes accompanied by a slight rigor; a catch in this region during inspiration; excessive flatulence and belching; "bilious attacks," and at intervals perhaps a faint icteroid tinge in the skin without definite jaundice; a perceptible increase in the tension of the upper right rectus muscle as compared with its fellow; indigestion, so-called, not definitely associated with the taking of food (in my series 64.7 per cent. had "indigestion" of varying degrees either before suffering from acute attacks or in the interval), all these are highly significant of beginning disease of the bile passages. I will grant that such symptoms do not at once call for operation, but they call for most careful supervision, and not the casual notice with which the profession has to its disgrace hitherto treated them, until the laity have come to disregard such symptoms and often fail to seek the advice by which many cases could be aborted.

This is the field for medical therapy, for Carlsbad treatment if the patient can afford it, not those later complicating conditions, the treatment of which by the physician is no more promising or rational than is that of the quack who either dissolves the stones or evacuates them in the form of soap-balls after huge doses of oil.

The time of election for operation is when medical treatment fails to control the inaugural symptoms previously mentioned or when they recur after supposed cure. Failing this, we have introduced into the situation an almost innumerable variety of factors dangerous to the patient's health and life, and for the surgeon a source of difficulty, of mental anxiety, and disaster to his ambition for enticing statistics. The most common result of infection is gallstones. The mild cases of infection are more dangerous in this respect than are the acute infections, for it is the low-grade catarrhal inflammation which causes desquamation of the lining epithelium, the production and deposit of cholesterin and biliary salts which result in stone formation, while more virulent processes do not at once cause stones, though they do give rise to other and perhaps more dangerous conditions. Later, when the

process becomes subacute or chronic, stones may be found, though not invariably. So long as the calculi remain in the gall-bladder the conditions are still practically ideal for operation. It is their further wanderings into the cystic, common, or hepatic ducts that give trouble alike to surgeon and patient.

The next complicating factor in order of frequency is adhesions. In this series they were present in about one-half the cases (45.4 per cent.). They are the result of pericholecystic or periduodenal inflammation. They are conservative so far as life is concerned, but they are often destructive to function. As I stated some years ago, "In many cases the symptoms and gravity of gall-bladder lesions are due not to the gall-bladder affection *per se*, but to the accompanying adhesions."

I believe that pericholecystic adhesions the result of gall-bladder and duct infection often give a clinical picture which is identical with that found in gallstone disease, and do so in the entire absence of gallstones at any time, and after operation they are capable of causing symptoms which mimic gallstone colic. In one case in this series the duodenum was constricted almost to the point of absolute obstruction by a band emanating from a previous infection of the gall-bladder, and in another the outer portion of the wall of the duodenum was invaginated and adherent. Aside from certain congenital abnormalities of the peritoneal attachment, adhesions in the abdomen are always the result of inflammation, and they may give rise to the most baffling but distressing symptoms. Abdominal adhesions are very unsatisfactory material for surgical treatment, since they are apt to reform after operation, and it is largely a matter of chance whether their new situation will be any more favorable for the patient. Hence the importance of eliminating by early operation this source of dissatisfaction with operative results.

It is impossible in a short paper to treat fully of the various clinical results of these processes. Ulceration, infiltration, perforation, gangrene, cicatricial contraction, and stenosis all are common, and affect in various degrees the different portions of the gall-bladder and ducts. In one case I observed a spontaneous cholecystogastrostomy in the process of making, a stone being still lodged in the opening from the gall-bladder to the stomach. In another case stones were embedded in the stomach wall, which had not been perforated. In still another instance the patient came with a sinus in the right side of the abdomen, which had discharged gallstones, Nature thus having effected what the surgeon could have done before with far greater safety to the patient. To permit such conditions as this to arise may be called conservative treatment, though just what it conserves is a mystery. In this field if not in politics we should all be progressives.

Last and not least we may have as a result of gall-bladder infec-

tions, or as a result of the same infection attacking the pancreatic tract, a pancreatitis, acute or chronic. Acute pancreatitis demands consideration as a separate clinical entity. But chronic pancreatitis is so often found coexistent with biliary infection that it may truly be considered as a part of the clinical picture of biliary infection. It is unlikely that pancreatic lesions are the result of direct extension of infection up the pancreatic ducts. Far more important it has seemed to me, is the extension by way of the lymphatics. The hardening of the head of the pancreas so often noted during operations on the biliary tract is due in its earliest stages at least to lymphatic infection and congestion, and is possible of relief by drainage. Our views concerning the nature of these swellings of the pancreas and their origin have been set forth in an article by myself and my assistant, Dr. Pfeiffer, in the AMER. JOUR. MED. SCI., 1912, cxliii, 4, 473. How important is the early relief of this condition must at once be evident. To restore a chronicly diseased pancreas to normal after the deposit of dense fibrous tissue is impossible by any means now at our command. Most if not all of these instances of pancreatic change which have been so wonderfully benefitted by operative procedures must have belonged properly in the category of pancreatic lymphangitis, and were not, properly speaking, cases of chronic pancreatitis.

But, nevertheless, it seems likely that such a pancreatic lymphangitis is the forerunner of a true chronic pancreatitis and if we are able to cure the underlying condition we may be said to cure the final one by preventing it. In this sense I believe that diabetes is at times a surgical condition While the pancreatitis induced by infections of the type under discussion does not often destroy sufficient of the islands of Langerhans to cause diabetes, there is sufficient clinical and pathological evidence that it may do so, and thus a timely operation may be the means of avoiding this dangerous condition. I have on more than one occasion seen glycosuria clear up after a successful drainage of the infected biliary and pancreatic ducts.

It is evident then that by timely operative procedures upon the biliary passages we are able to do far more than simply to remove a few gallstones or loosen a few adhesions. We are able to apply the principle of drainage to infections here as in other parts of the body, to cure first causes, to do away with the harmful results of invasion by pathological bacteria.

Aside from traumatic and neoplastic affections of the biliary ducts the conditions calling for surgery may be grouped as follows: (1) Non-calculous cholecystitis, (2) calculous cholecystitis and its complications, (3) pancreatic disease.

In non-calculous cholecystitis there is but one problem—to remove the results of inflammation and to insure sufficient drainage for a proper length of time. The gall-bladder may require

removal if gangrenous or inordinately thick and functionless, though I attempt to preserve it in all cases.

Pancreatic disease furnishes a strong indication for temporary or permanent drainage of the biliary tract, temporary by direct tube drainage or permanent by some form of anastomosis between the biliary system and the alimentary canal to give greater drainage than the natural outlet affords. In my practice this has generally consisted of cholecystoduodenostomy.

Of the methods of treatment of pancreatic conditions found at operation I shall speak more at length later.

Kocher's oft-quoted remark that "Gallstones belong neither to the surgeon nor to the physician, they belong to the patient," is quite correct. It is, indeed, the patient's privilege to have his bodily ailments treated in such manner as he sees fit. Yet were every gallstone patient informed of the possible results of his condition, and shown the difference between the mortality and end results in early and late operations, there is but little doubt in my mind that he would quickly turn to surgery for relief.

What, then, are the indications for operation in diseases of the biliary ducts and gall-bladder? (1) More than one attack of true biliary colic; (2) symptoms suggestive of upper abdominal adhesions and chronic biliary insufficiency; (3) hydrops of the gall-bladder; (4) obstruction of the common duct; (5) the occurrence of acute infections complicating previously existing biliary disease; (6) the evidences of pancreatic disease, acute, subacute, or chronic.

No physician or surgeon of the modern school expects to see more than a fraction of his gallstone patients come to him with a history of biliary colic. Numbers, indeed, give a fair approach to a classical history of gallstones, but the majority give a far vaguer combination of symptoms often with, but at times without, any history of jaundice.

In comparison with the total number of cases suffering from gallstones or their effects, classical cases are few. I sometimes think that the simple rule "fair, fat, and forty, and belches gas," would be a safer maxim for our students if we wish them to recognize gall-bladder disease than is the hard and fast clear-cut picture so faithfully embalmed in most of our text-books.

Just a word about the age at which the gall-bladder is likely to be infected. We have been taught that it is a disease of the later years. The average age of the 142 patients was 40.8 years. The average duration of symptoms was 6.6 years. On the average, then, these patients were but thirty-four years of age when known to be infected. In other words, the begining of the condition is in early adult life, and the reason why it has been considered a disease of the declining years is because the early symptoms go unrecognized until the accumulation of pathology forces a diagnosis and treatment. Six and one-half years is too long for the

physician to ponder over a case that is trending toward operation as the only means of relief. An interesting feature of cholelithiasis is the liablity to recrudescence after labor. In the present series there are 3 instances of gallstone colic following immediately after parturition. All had had symptoms of gall-bladder disease previous to the last pregnancy. These attacks were the most severe that the patients had experienced.

Pain that could be called biliary colic was present in 80 per cent. of the cases; jaundice in 47 per cent. These percentages are high in any operative series, since they are striking, severe, and of an order to induce the patient to seek operative relief. Bearing this in mind it is apparent how relatively infrequent a symptom of gallstones these vaunted symptoms really are. A low incidence of these symptoms in the operative figures of a surgeon is a tribute to the intelligence of the profession among whom he labors.

The second group of these cases in which I consider operation indicated, that is, those with symptoms of upper abdominal adhesions and chronic biliary insufficiency, is a large one. It includes many gallstone cases and others of non-calculous cholecystitis and cholangitis which in former years would have been called symptomless because of the absence of pathognomonic signs. And although we find in these patients no such absolute indication for operation as the occurrence of biliary colic, yet I maintain that a carefully taken history will localize the trouble in the biliary tract and that the surest cure is drainage.

Hydrops of the gall-bladder and obstruction of the common duct give symptoms which are quite definite and well known, and it is necessary only to mention these conditions to make our statement of operative indications complete. It must not be forgotten that one or more stones may be present in the common duct without causing jaundice, and it has been my experience to find this condition in 3 out of 32 cases operated upon in the University Hospital in the last year and a half. Needless to say this is the most favorable time for operation upon stone in the common duct.

In common duct obstruction I prefer to operate in the interval between attacks of complete occlusion. What surgeon does not prefer to have his patient in the best possible condition for operation? I take issue, however, with those surgeons who, seeing a patient during acute obstruction, decide to wait until the obstruction has been relieved before operating. This may be good for the surgeon's results, since he is relieved of the necessity of operating upon certain of the more severe cases who will seek operation elsewhere when the condition instead of improving becomes worse.

I do not, of course, advocate operation in every case of acute obstruction of the common duct during the attack of colic nor during the few days immediately following, but I do not always wait for the subsidence of jaundice, for at times this does not occur

until the patient is emaciated and weakened in the extreme, to say nothing of the adhesions, etc., generated by the infection. The time to be of most service to a patient with obstruction of the common duct is during the existence of the obstruction when by operation we may come to the rescue of the liver and inflamed bile passages. After the first few days there is no greater danger of causing infection of the peritoneum than subsequently. Hemorrhage, one of the greatest dangers, does not occur in the early stages but only in the cases where a cholemic state has existed for a long time. In all cases where I fear hemorrhage I fortify the patient with injections of blood serum preferably obtained from a healthy member of the family. Large doses should be used—from 50 to 200 c.c. given subcutaneously. I believe serum is of value in this connection. Human serum is preferable to that of the horse or other animals, for obvious biological reasons. Gelatin is useless for the prevention of capillary oozing, and the salts of calcium, while they may effect a reduction in the coagulation time of the blood, do not appear to have much influence upon cholemic hemorrhage.

The evidence of pancreatic disease points also directly to the need for operation. Unfortunately it is most difficult to be sure of this condition. Chronic pancreatitis, so often associated with disease of the biliary tract, only occasionally gives rise to symptoms which could not just as well be accounted for by gallstones or chronic non-calculous cholecystitis.

When, however, the character of the stools, with an intermittent diarrhea and constipation, and those grave metabolic changes attributable to pancreatitis, give evidence of pancreatic disease, I consider operation indicated even in the entire absence of symptoms pointing to disease of the biliary tract. Particularly is this true when to the symptoms mentioned we have added a glycosuria. In the present series the pancreas showed recognizable lesions chiefly of the nature of pancreatic lymphangitis in 45 cases (32 per cent.). In 3 of these there were some flecks of fat necrosis in the vicinity revealing the presence of an acute exacerbation of the chronic inflammation.

I have had the Cammidge "C" reaction performed in 84 cases of the present series, with the following results: Pancreas involved—Cammidge positive, 9 cases, Cammidge negative, 20 cases. Pancreas uninvolved—Cammidge positive, 8 cases, Cammidge negative, 48 cases.

This is a poor showing for a pathognomonic reaction, and I can therefore place no dependence in it, as these results substantially correspond with about 400 previously obtained in the laboratory of the German Hospital in these and other conditions.

Operation must accomplish three things: (1) It must meet the actual pathological condition and relieve it; (2) it must remedy

if possible the underlying cause; (3) it must if possible prevent a recurrence of the conditions found by rendering the return of the cause unlikely.

The actual pathological conditions met with in surgery of the bile ducts consist of three great groups: (*a*) Infection; (*b*) calculi; (*c*) of adhesions about and malformation of the gall-bladder and ducts as a result of infection.

Gallstones when found are to be removed, of course, it matters not in what part of any duct they may be, and it is, as a rule, possible to do this if the operator be competent and patient. Their removal from the gall-bladder and cysticus is generally a matter of small difficulty, unless the stones are very small and buried within the mucosa of the gall-bladder or in a diverticulum.

The removal of a stone from the choledochus is often a matter of great difficulty, particularly if it be situated in the pancreatic or the intraparietal portion of the duct. When the stone is in the first portion of the common duct, or can be pushed into it, the method of removal consists in direct incision of the duct over the stone and its removal. When the stone is in the second or third portion of the duct an effort should be made gently to bring it up into the more accessible supraduodenal portion of the duct, or failing in this, to dislodge it into the duodenum. Retroduodenal and transduodenal methods of approaching a stone in the common duct are distinctly more dangerous than simple choledochostomy, and only very rarely necessary. At times a soft stone which is lodged in the lower extremity of the duct may be broken up and removed piecemeal with the gallstone scoop. I am never satisfied until I can pass the olive pointed end of a good sized gallstone explorer through the papilla of Vater into the duodenum. Stones which have worked their way upward into the hepatic ducts are very difficult and at times impossible of extraction. These are one cause of the recurrence of symptoms after the removal of common duct calcul , and is a possibility that we cannot control. As a rule the downward flow of bile keeps the stones in the lower duct where they can be removed.

A point of some importance in connection with surgery of the common bile duct is a variation from the normal in the formation of the choledochus in which the cysticus and hepaticus join near the duodenum, and the hepatic duct entering posteriorly appears much as a branch of the cystic duct, the latter seemingly being continued directly into the common duct.

In addition to the removal of gallstones in calculous cases we must make certain that embarrassing pericholecystic adhesions are freed. It is not always advisable to release all the adhesions when the lesion can be satisfactorily dealt with without doing so. The continuity of the bile passages must be established or provision made for the proper discharge of the bile.

The removal of adhesions and attention to the state of the biliary ducts constitute also the main features in surgery of the actual pathology of non-calculous cholecystitis, which presents in every way the problems of gallstone disease minus only the actual presence of the stones.

The remedying of the underlying cause of disease of the biliary system, when not malignant, depends upon our ability to combat infection in this field. Since infection is the direct causative factor in all the lesions with which we have to deal, it is only when we successfully meet it that we can be certain that everything possible has been done for the relief of the patient.

And, as in infection in any other part of the body, our reliance must be upon drainage, this must be our watchword particularly in biliary surgery, for since infections here are so persistent in their course and insidious in their harmful action, it is essential that nothing be left undone for their final cure.

I believe, therefore, that in every operation upon the gall-bladder it should be drained, granting that the viscus is not diseased to the extent of being rendered functionless.

Drainage of the common duct is imperative when we have opened it for stone, in all grades of cholangitis and particularly after cholecystectomy in the presence of liver infection and pancreatic involvement, even when there are no stones in the duct. H. Kehr[2] recommends that the choledochus be drained after cholecystectomy when there is: (1) Thickening of the pancreas, especially of the head; (2) when the chloedochus is thickened and distended; (3) with a history of icterus, chills, and passing of stones; (4) when a considerable amount of the cystic duct is left and it is split to the common duct; (5) when many small stones are found in the common duct; (6) drainage of the hepaticus when cloudy pus oozes from the stump of the cystic duct, proving infection of the choledochus; (7) in the presence of liver enlargement, indurated liver, and cirrhosis.

With these indications for common duct drainage after cholecystectomy I fully agree.

All cases of infection of the biliary passages, unless very transient or coming as intercurrent affections in acute illness, demand drainage of the gall-bladder. Of these any that show marked infection or a cholangitis demand common duct drainage also.

For stone in the gall-bladder I consider cholecystostomy the best operation. It has a slightly lower mortality, is followed by fewer adhesions than cholecystectomy, and leaves the gall-bladder as a possible future drainage outlet in case of serious biliary or pancreatic disease. Excision of the gall-bladder I practise in cases of: (1) Malignancy; (2) hydrops of the gall-bladder; (3) chronic empyema of the gall-bladder; (4) gangrene; (5) when the cystic

[2] Arch. f. klin. Chir., 1912, v. 97, 2, p. 301.

duct is not patulous; (6) when many small calculi are imbedded in the gall-bladder mucosa.

When in the course of an operation upon the biliary tract we find a pancreatic lymphangitis or a beginning pancreatitis drainage is invariably indicated. If the gall-bladder is greatly diseased and full recovery doubtful in a case complicated by pancreatic lymphangitis, I consider it an indication for cholecystectomy. Drainage of the common duct should then be established. There is no doubt that the pancreas may be drained through the opening in the common duct, as I have noted the peculiar irritating character of the discharge in certain of these cases. In an instance seen within the last month the patient's skin was severely excoriated by contact with the discharge from the common duct, and the presence of pancreatic ferment was proved by the digestion of blood serum and starch in alkaline solution. In this case I had passed a good-sized gallstone explorer through the ampulla of Vater and had no doubt of its patency. When the pancreatic duct does not open into the sinus of Vater, of course this avenue of drainage of the pancreatic secretion is not possible; but the operation is still productive of good in that the primary focus of infection in the gall-bladder is abolished.

If the lesion be primarily of the biliary ducts, common duct drainage will be sufficient, though temporary, to meet the indications furnished by the pancreatic condition.

If the pancreatic condition be the main one or is the one causing symptoms, permanent drainage by a cholecystoduodenostomy is indicated, and it has been a procedure most brilliantly effective.

The surgery of the biliary tract has been made satisfactory from the standpoint of operative mortality and end results.

In conclusion let me again urge the danger of procrastination and too much deliberation. It is well known that he who deliberates is lost, but under these circumstances it may be the unhappy lot of the patient to be numbered among the lost. It should be mortifying to the physician to see the disastrous results of infection laid bare, to say nothing about the mortification of the patient. The full story of the autopsy *in vivo* has not yet been told. The new pathology is now being written.

The dawdling with duodenal buckets, fallacious laboratory methods, etc., I deplore; and could patients be educated to their uselessness, they, too, would despair. The resources of surgery are rarely successful when practised upon the dying, nor are they so uniformly successful when pathology is advanced as when it is in its incipiency.

At least nine-tenths of the mortality of operation so-called is in reality the mortality of delay. Bearing this in mind, we must place the problem of the reduction of invalidism and death due to biliary infections in the hands of him who sees the patient first, namely, the family physician.

A CRITICAL STUDY OF OXYURIS AND TRICHOCEPHALUS APPENDICITIS.

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In previous reports we have attempted to draw a brief clinical picture of oxyuris and trichocephalus appendicitis and to demonstrate the pathology of the disease. In the present paper we wish to review the literature of the subject and to attempt by an analysis of it and of our own cases to identify parasitic appendicitis as a separate disease having an etiology, pathology, and symptomatology of its own. We are considering only Oxyuris vermicularis and Trichocephalus trichiura in relation to appendicitis, because they have been the two parasites most frequently associated with this disease and because the lesions and symptoms which they produce are, in a general way, similar. In the following pages we will not attempt to separate the oxyuris from the trichocephalus cases except in the section on pathology.

Incidence. The first reports which we can find of clinical cases of appendicitis in which the removed appendix contained oxyuris or trichocephalus were published in 1900 by Beyea,[6] Frazier,[21] and Guinard,[26] the first two writers reporting oxyuris, and the last trichocephalus. Still,[54] however, in 1899 described oxyuris in the appendices of children at autopsy. Shortly after this, in 1901, Metchnikoff[41] reported 3 cases of appendicitis due to Ascaris lumbricoides. It was this paper which served to awaken interest in parasitic appendicitis, for it was immediately followed by a series of articles, some mere case reports, others discussing more or less fully various phases of the subject. It is interesting to note the incidence in various countries of oxyuris and trichocephalus in the feces, in the intestinal tract and appendix at autopsy, and in resected appendices. In France the figures vary. Brumpt and Lecene[8] (Paris) state that in 10 per cent. of the appendices of adults coming to autopsy either oxyuris or trichocephalus are found. A year later Brumpt[7] (Paris) reports finding oxyuris in the appendix in 3.5 per cent. of 800 autopsies. In 13 autopsies on children he found oxyuris in the appendix twice (15 per cent.). In the surgical clinic of August Broca oxyuris was present in the appendix in 24 out of 60 cases of appendicitis operated on, or 40 per cent. Railliet[49] (Paris) examined 119 resected appendices and found oxyuris in 48.74 per cent. In one case trichocephalus was also

present. Oelnitz,[45] at Nantes, observed 21 cases of appendicitis, in 18 of which trichocephalus eggs were found in the stools. Martin[40] says that in Montpelier oxyuris was found only once in 500 resected appendices, and then quotes a personal communication from Vedel, who states that, in 1900–1901, 50 per cent. of the cases of appendicitis at Montpelier had trichocephalus in their stools. In Germany Hoepfl[32] reports finding oxyuris in 24 out of 117 resected appendices, or 21 per cent. Delsmitt[17] examined the feces of 21 children who had appendicitis, and in 18 of them found eggs of either trichocephalus or ascaris. Oppe[46] reports finding oxyuris in 5 out of 60 resected appendices, or 8.3 per cent. Still[54] (London) in 200 autopsies on children under twelve years of age, found thread-worms in the intestines in 19 per cent. of the cases; in children between two and twelve years of age, 32 per cent.; in 6 cases they were found only in the appendix. Matigum during four and a half years in China, where intestinal parasites are very common, saw only 1 case of appendicitis, and that appendix showed no worms. Treille[56] reports similar findings in Algiers.

In the United States the subject seems to have been largely overlooked. Crile[13] summarized "1000 cases of appendicitis with observations on etiology," and fails to mention worms of any sort. Deaver[16] found oxyuris once in 500 appendectomies on children. Hanley[29] reports finding at operation an appendix filled with pinworms, and says it is the first he has seen in 500 appendectomies. Kelly[36] examined 460 cases of appendicitis, with special reference to pathogenesis, but fails to enumerate worms as a possible etiological factor. Erdman[19] found pin-worms in 4 out of 250 children's resected appendices. In New York, Schloss[53] examined the stools of 280 consecutive children and found that 11.07 per cent. carried trichocephalus and 8.21 per cent. oxyuris. It is interesting to note that in 3 of these cases (all oxyuris) the patients complained of abdominal pain, 2 of them localizing it on the right side.

Our material has been obtained largely from the two surgical services of the Presbyterian Hospital, a small part of it coming from other hospitals in New York, and one appendix from a neighboring town. The material consists of 148 unselected appendices of children aged between two and fifteen years, 129 being clinical and 19 of them autopsy cases. We have also studied 4 adult appendices infested with oxyuris.

Of the 129 clinical cases, 19 of them, or 15 per cent., contained either oxyuris or trichocephalus; 89 appendices of the series were gangrenous or suppurative in type. In these we found parasites only 4 times, or in a fraction more than 4 per cent. In the non-suppurative cases parasites were found 15 times, or in about 38 per cent. While we have made no attempt to determine the incidence of the disease in adults, we have encountered 4 adult cases, and these we include in our report. In 19 appendices obtained

at autopsy upon children aged between two and fifteen years, we have found worms in 3, or about 15 per cent. We believe, however, that if the autopsy series could have been as large as the series of clinical cases, the incidence of parasites in the normal appendices of children would be much smaller than 15 per cent.

We have been able to collect from the literature 49 definite case reports of appendicitis associated with oxyuris or trichocephalus. To this list we have added 23 of our own cases, making a total of 72 reported cases. In the table we have given a brief outline of each case. In 61 of these the age is stated. Fig. 1 shows graphically the large proportion of cases in young people. A little over 50 per cent. occurred between the ages of six and fifteen years. The youngest case in our own series was a boy, aged three years, and our oldest case, a woman, aged fifty-four years. Kornbluh[38] has recently reported a case in a child, aged twenty-one months.

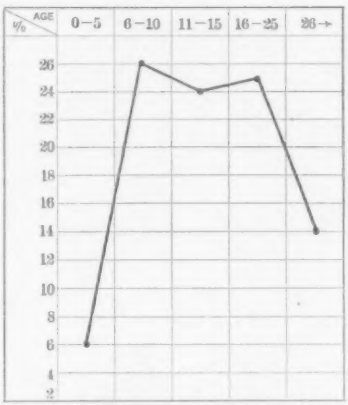

FIG. 1.—Showing the relation of age to incidence in 61 reported cases of oxyuris and trichocephalus appendicitis.

In 68 cases the sex has been stated. There were 23 males and 45 females, or about 2 females to each male.

The disease occurs in both city and country, and is by no means limited to the poorer classes. The majority of our own cases have come from tenement districts, a few from the more wealthy residential sections of the city. It will be noted that according to our figures the incidence of parasites in the diseased appendix is lower in New York than it is in French and German cities. The prevalence of oxyuris and trichocephalus in France and Germany is well known. It is proable that the incidence is higher in New York and other American cities whose population is largely foreign than it is in the smaller towns and country districts whose inhabitants are for the most part native-born Americans.

Cases of Oxyuris and Trichocephalus Appendicitis.

Case No.	Reported by	Age.	Sex.	Type of appendicitis.	Parasite.	Number of parasites.			Number previous attacks.	Pain.	Vomiting.	Tenderness.	Rigidity.	T.	P.	R.	Leukocytes.	Polynuclears.	Result.
						Total.	M.	F.											
1	Allen	11	F.	Catarrhal	Oxyuris	12	..	..	0	+	+	+	+	103.0	120	..	.....	...	Cured.
2	Ashhurst	14	F.	Acute suppurative	Oxyuris	..	..	..	0	..	....	....	....	100.6	88	34	25,000	...	
3	Bégouin	24	F.	Catarrhal	Oxyuris	150	..	..	Many for 5 years	+	....	+	....	N.					
4	Beyea	22	F.	Catarrhal	Oxyuris	1	..	..	1	..	....	++	....	...	..	..	....	...	Cured.
5	Brumpt and Lecene	10	M.	Catarrhal	Oxyuris	Many	..	..	2	..	+	+	....	+	100				
6	Carson	19	F.	Catarrhal	Oxyuris	1	0	1	0	+	+	+	Absent	103.8	116	32	....	...	Cured.
7	Carson	24	F.	Catarrhal	Oxyuris	3	..	..	1	+	....	+	Absent	100.6	118	28	....	...	Cured.
8	Culhane	21	F.	Catarrhal	Oxyuris	18	..	..	....	+	+	+	+	...	..	..	....	...	Cured.
9	Cuthbertson	45	F.	Catarrhal	Oxyuris	Many	..	..	0	+++	....	....	+++	99.0 to 103.0					
10	Dooley	Adult	F.	Catarrhal	Oxyuris	20	..	..	0	+	+	+	+	N.	..	..	....	...	Cured.
11	Frazier	2	F.	Catarrhal	Oxyuris	Many	..	..	1										
12	Galli-Valerio	5	M.	Gangrenous	Oxyuris and trichocephalus	Many	..	..	....	+	+	....	....	...	..	..	....	...	Died.
13	Garrod and Fairbanks	10	M.	Catarrhal	Oxyuris	++	..	..	....	..	....	....	....	103.0	..	..	26,000		
14	Girard	8	F.	Catarrhal	Trichocephalus	2	1	1											
15	Guinard	25	F.	Catarrhal	Trichocephalus	1	..	..	0										
16	Guinard	..	F.	Catarrhal	Trichocephalus														
17	Hall	24	M.	Catarrhal	Oxyuris	+	..	..	....	+	....	+	....	N.	..	..	....	...	Cured.
18	Hanley	35	F.	Catarrhal	Oxyuris	++	..	..	0	+									
19	Heekes	31	F.	Catarrhal	Oxyuris	11													
20	Hippius and Lewenson	6	F.	Catarrhal	Oxyuris	80	Few	Many	For 3 years	+	+	+							
21	Hubbard	9	F.	Gangrenous	Oxyuris	2	..	..	0	..	....	....	....	N.	..	..	....	.,.	Died.
22	Hutchinson	?	F.	Catarrhal	Oxyuris	++													
23	Kablukoff	?	?	Catarrhal	Oxyuris	4													
24	Kelly and Hurdon	12	F.	Catarrhal	Oxyuris	++	..	..	0	+	....	+	+	102.0	120	..	20,000		
25	Lediard	7	F.	?	Oxyuris	..	..	..	0	+	+	+	....	103.0	..	..	++		
26	Lediard	30	M.	Catarrhal	Oxyuris	3	..	..	....	..	....	+							
27	Martin	?	M.	Gangrenous	Trichocephalus	..	..	..	....	..	....	....	....	...	..	..	....	...	Cured.
28	Martin	25	M.	Catarrhal	Oxyuris	++	0	..	For 5 years	+	Nausea	+	None	...	..	..	....	...	Cured.
29	Mayo	?	F.	?	Oxyuris	..	..	..	....	..	....	....	....	...	..	..	....	...	Cured.
30	Monash	23	F.	Catarrhal	Oxyuris	..	..	..	+++	+	+	+	+	N.	..	..	7,200	...	Cured.
31	Monash	14	F.	Catarrhal	Oxyuris	36	..	..	For 2½ years	+	+	+	Slight	...	..	..	....	...	Cured.
32	Moore	23	M.	Catarrhal	Trichocephalus	1	..	..	0										
33	Morkovitine	22	M.	?	Oxyuris	12													
34	Pabeuf and Du Bois	20	F.	Catarrhal	Oxyuris	..	..	..	For 3 years										
35	Peraire	29	F.	Catarrhal	Oxyuris	1	..	..	....	+	+	....	....	+					
36	Rammstadt	20	M.	Catarrhal	Oxyuris	++	..	..	++	+	+	....	....	...	86	..	?26,000		
37	Romanovitch	13	F.	Catarrhal	Oxyuris	12	..	..	....	+	+	....	....	N.					
38	Thrush	20	F.	Catarrhal	Oxyuris	++	..	..	For 6 months	..	....	....	....	...	..	..	....	...	Cured.
39	Vigouroux and Collet	?	?	Acute suppurative	Trichocephalus	1													
40	Von Moty	19	M.	Catarrhal	Oxyuris	..	..	..	For 5 years	+									

40	Von Moty	19	M.	Catarrhal	Oxyuris	..	..	..	For 5 years	+									Cured.
41	Von Moty	Adult	M.	Catarrhal	Oxyuris	5	..	..	For 2 years	+									Cured.
42	Von Moty	Adult	M.	Catarrhal	Oxyuris	2													
43	Von Moty	?	M.	Gangrenous	Oxyuris														
44	Von Moty	10	M.	?	Oxyuris	..	..	..	....	..	....	....	....	...	..	..	....	...	Cured.
45	Wakefield	17	F.	Catarrhal	Oxyuris	6-8	..	..	....	..	....	....	....	...	..	..	....	...	Cured.
46	Walther	Adult	F.	Catarrhal	Trichocephalus	1	..	..	....	+	....	....	....	...	..	..	....	...	Cured.
47	Weinberg	11	M.	Catarrhal	Oxyuris	1	..	..	0	0	0	+	0						
48	Weinberg	38	F.	Catarrhal	Trichocephalus	1	0	1	....	+	....	....	+	104.0	130	..	....	...	Died.
49	Winkler	7	?	Catarrhal	Oxyuris	1													
50	Cecil and Bulkley	9	F.	Catarrhal	Oxyuris	17	14	13	0	+	+	+	+	102.5	120	24	18,000	42%	Cured.
51	Cecil and Bulkley	12	F.	Catarrhal	Oxyuris	28	19	9	0	+	+	+	+	100.0	..	..	16,000	87%	Cured.
52	Cecil and Bulkley	14	F.	Catarrhal	Oxyuris	35	5	30	2	+	+	+	+	101.6	104	22	....	...	Cured.
53	Cecil and Bulkley	3	M.	Catarrhal	Oxyuris	1	0	1	0	0	0	0	0	98.0	90	24	....	...	Cured.
54	Cecil and Bulkley	14	M.	Catarrhal	Oxyuris	1	0	1	1	+	+	+	+	98.0	80	20	....	...	Cured.
55	Cecil and Bulkley	43	F.	Catarrhal	Oxyuris	6	3	3	0	+	+	+	Absent	100.0	92	24	8,500	62%	Died.
56	Cecil and Bulkley	10	F.	Catarrhal	Oxyuris	3	2	1	0	+	+	+	Absent	99.0	136	36	18,000	81%	Cured.
57	Cecil and Bulkley	6	F.	Catarrhal	Oxyuris	1	1	0	0	+	+	+	Very slight	100.0	140	22	6,600	76%	Cured.
58	Cecil and Bulkley	8	F.	Catarrhal	Oxyuris	4	2	2	0	+	+	+	+	102.0	..	..	....	...	Cured.
59	Cecil and Bulkley	8	F.	Catarrhal	Oxyuris	5	2	3	0	+	+	+	+	102.0	..	..	....	...	Cured.
60	Cecil and Bulkley	7	F.	Gangrenous	Oxyuris	14	2	12	0	+	+	+	+	102.0	140	30	44,000	88%	Cured.
61	Cecil and Bulkley	14	M.	Gangrenous	Oxyuris	1	1	0	0	+	+	+	+	99.5	..	..	9,000	83%	Cured.
62	Cecil and Bulkley	14	F.	Gangrenous	Oxyuris	2	1	1	0	+	+	+	+	103.0	110	24	21,000	92%	Cured.
63	Cecil and Bulkley	10	M.	Catarrhal	Oxyuris	19	7	12	For 5 months	+	Absent	Slight	Absent	101.0	128	28	....	...	Cured.
64	Cecil and Bulkley	54	F.	Catarrhal	Oxyuris	6	3	3	0	+	0	0	0	99.0	80	20	10,500	74%	Cured.
65	Cecil and Bulkley	37	F.	Catarrhal	Oxyuris	5	3	2	6	+	+	+	+	...	..	..	9,500	77%	Cured.
66	Cecil and Bulkley	15	F.	Catarrhal	Oxyuris	1	0	1	1	+	+	+	+	99.0	..	..	21,000	76%	Cured.
67	Cecil and Bulkley	23	F.	Catarrhal and chronic obliterating	Oxyuris	3	2	1	0	+	0	+	Absent	99.0	90	20	21,000	78%	Cured.
68	Cecil and Bulkley	5	M.	Catarrhal	Oxyuris	7	7	0	0	+	+	0	Absent	101.5	126	24	....	...	Cured.
69	Cecil and Bulkley	15	F.	Catarrhal	Oxyuris	2	1	1	0	+	0	+++	Absent	100.0	90	20	10,000	76%	Cured.
70	Cecil and Bulkley	13	M.	Catarrhal	Oxyuris	1	0	1	0	+	Nausea	+	Absent	100.0	80	20	10,000	70%	Cured.
71	Cecil and Bulkley	7	M.	Gangrenous	Trichocephalus	1	1	0	0	+	+	+	+	103.0	120	24	22,000	93%	Cured.
72	Cecil and Bulkley	12	..	Catarrhal	Trichocephalus	1	1	0											

PATHOLOGY.[12] 1. The *Parasite. The* oxyuris is by far the most common parasite found in the appendix. Of the reported cases, 61, or 84 per cent., contained oxyuris, 10 or 13 per cent. trichocephalus, and in 1 case both parasites were found in the same appendix. In 28 cases the sexes of the parasites have been noted. In 10 cases the male predominated, in 11 cases the female, and in 7 cases the sexes were equally represented. Railliet,[49] however, states that the female predominates in three-fifths of the cases. The number of parasites found has varied from 1 to 150, the average being about 11. Oxyurides in various stages of development have been found (Hippius and Lewinson) not only in the lumen, but also in the walls of the same appendix, and from this Still argues that the worms must have been hatched in the appendix, and that the appendix can therefore serve as a breeding place for the pin-worm. In appendices containing trichocephalus there is as a rule only one parasite found.

There has been much discussion in the literature as to whether oxyuris or trichocephalus can be the exciting cause of appendicitis, or whether they act merely as foreign bodies and so by injuring the mucosa of the appendix form a *locus minoris resistentiæ* through which bacteria may enter and do the actual harm. That oxyuris and trichocephalus can penetrate the mucous membrane has been shown in a number of recently reported cases (Brumpt and Lecene,[8] Galli-Valerio,[22] Hippius and Lewinson,[31] Romanovitch,[51] Ruffer,[52] Unterberger,[57] Wagener,[61] Wakefield,[62] Walther,[63] Weinberg,[64] Winkler[65]), and we have obtained from our own cases many sections showing the parasites beneath the mucosa. Brumpt suggests that the oxyuris punctures the mucosa for blood, but Railliet states that he has never seen blood in the body of the worm, and the parasite fails to give a reaction for iron (Unterberger). Askanazy,[4] however, obtained a positive reaction for iron in the body of the trichocephalus, and showed that it penetrated the mucosa and sucked blood from the host. The cases of Ruffer, Wagener, and Hippius and Lewinson show that the oxyuris does lay eggs beneath the mucosa, but while it may be for this object that the pin-worm sometimes burrows, this is not its sole purpose, for in many of the reported cases, and in a majority of our own cases, only the male parasite has been found beneath the mucous membrane. It is possible that the oxyuris feeds only on the blood plasma of the host, and for this reason fails to give an iron reaction.

Various opinions have been advanced by different writers in the attempt to explain why the presence of trichocephalus or oxyuris in the appendix should cause symptoms of appendicitis or produce pathological lesions in that organ. Monash[44] suggests that the worms block the lumen of the appendix and that the contractions of the muscular wall in attempting to expel them give rise to appendicular colic, or that the irritating sharp tails of the female

initiate contractions of the appendix, thus causing colic. Oppe[46] thinks that the very presence of the oxyuris in the appendix may cause a colicky attack, the pain being due to the muscular contraction of the appendix on the worm as it tries to wriggle through into the cecum. He thinks that in this way the oxyuris may cause an attack of appendicitis and yet escape into the cecum and leave behind no trace of a lesion. Hubbard[33] goes so far as to state that there is no proof that oxyuris can cause appendicitis except in its role of a foreign body. These are the simplest of the many theories which place oxyuris in the class of foreign bodies.

The majority of writers admit that the worms puncture the mucosa, but beyond this point there is much disagreement as to whether the worms *per se* can cause appendicitis or whether they merely open the way for bacterial infection. All observers are agreed that the mucosa having been injured, bacteria may enter and set up inflammatory changes, and the majority of writers agree that an oxyuris or trichocephalus may in this way act as a predisposing factor as readily as any other foreign body. Prominent among the reports in the literature which prove this point are the cases of Girard,[24] Weinberg, and Galli-Valerio, in all of which marked zones of inflammation were found about penetrating parasites. That an oxyuris or trichocephalus can without secondary bacterial infection render an appendix pathological or be responsible for the classic symptoms of appendicitis is not universally admitted. From a study of our own cases and those reported in the literature, however, we are convinced that they are capable of such action. Hippius and Lewinson failed to find bacteria about penetrating oxyurides, although the parasites lay deep in the submucosa in sinuses which were lined in some places with necrotic tissue and in other places with young granulation tissue. In most of our cases in which we have found the worm embedded in the mucosa we have been struck with the absence of leukocytic infiltration about the parasite, and we have sections of appendices showing oxyurides curled up in lymph follicles around which there is neither inflammation nor necrosis. In other sections there is necrosis, but no infiltration about the invading oxyurides. Appendices infested with trichocephalus also usually fail to show any infiltration of leukocytes about the invading parasite. Examination of our specimens has convinced us that there is a definite disease of the appendix caused by Oxyuris vermicularis or Trichocephalus trichiura, and that these parasites can by their own action, irrespective of bacterial invasion, set up specific and peculiar lesions in the appendix.

2. *The Lesion.* In 66 of the 72 reported cases, including our own, the general pathological type of appendicitis has been stated or can be deduced from the context. Only 10 were of the gangrenous or suppurative variety, the remaining 58, or 86 per cent., being of a

catarrhal or non-suppurative type. Of our own 23 cases, 4 were gangrenous, 3 of these containing oxyuris, and the fourth trichocephalus. In only 1 of these 4 appendices were we able to find lesions definitely attributable to parasites. Of the remaining 19 non-suppurative appendices, we were able in 12 cases, to demonstrate microscopic lesions, which we consider pathognomonic for the parasites under discussion. Of the 7 negative cases, 4 were in adults and 3 in children. Over 4000 sections of these 7 appendices were prepared and examined but no characteristic lesions could be found. We were also unable to find lesions of any sort, parasitic or inflammatory, in our 3 oxyuris appendices obtained at autopsy. These all appeared normal in every respect except for the presence of oxyurides and swelling of the keim centres of the lymph follicles.

The following description of lesions is summarized from our previous pathological report and corresponds for the most part with that given by the writers above referred to. As the lesions produced by the oxyuris and trichocephalus differ somewhat, we will describe them separately.

Lesions Caused by Oxyuris. At operation the appendix may at first sight appear normal, but is usually found moderately swollen and rigid, with a serosa which is smooth, pale, and glistening. The vessels of the serosa may be congested. On opening the appendix the lumen usually contains a considerable amount of bloody mucus, in which the parasites may or may not be immediately visible. The mucosa is usually swollen, pinkish, and velvety. There are frequently seen scattered over it small red purpuric areas or minute hemorrhagic ulcers. There is usually no evidence of suppuration. The worms at times may be seen attached to the mucous membrane, and in 2 of our cases living worms were seen under magnification to free themselves from the mucosa. The microscopic lesions found may be divided into groups, according to the degree of damage which the parasite has done.

1. In the first group we have placed those appendices which, though containing parasites, fail to show changes other than those of a mild catarrhal nature. Externally the appendix appears as above described. The mucosa is thicker than normal, but shows no hemorrhagic foci, and the worms are seen to lie, unattached, in the lumen of the appendix. Fig. 2 shows a cross-section of such an appendix filled with oxyurides. The microscopic picture is that of a catarrhal inflammation, the crypts of the mucosa being distended with mucus and the keim centres of the lymph follicles enlarged. The other coats are usually normal, although a few scattered polymorphonuclear leukocytes, eosinophiles, and lymphoid cells may sometimes be seen. In this group we have placed 6 of our cases.

2. The second group includes those cases in which the mucosa has been penetrated by the oxyuris, but where little if any tissue

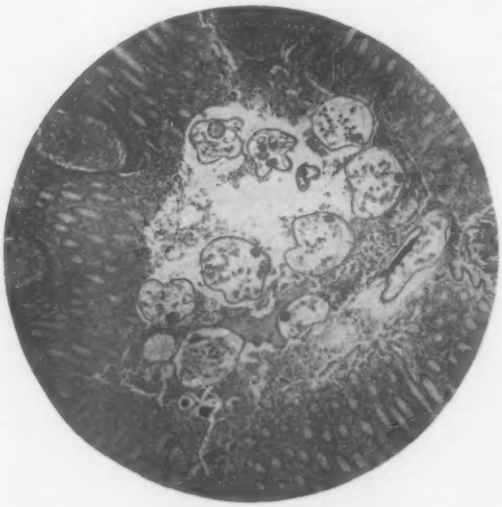

FIG. 2.—Lumen of appendix is filled with oxyurides, mostly females, whose uteri are distended with ova. Parasites separated by mucus and blood. × 50.

FIG. 3.—A male oxyuris is seen invading the mucosa through a break in the columnar epithelium. × 107.

has been destroyed. The parasite, usually a male, breaks through the epithelium and may or may not reach a lymph follicle. Fig. 3 shows an oxyuris invading the mucosa. Fig. 4 shows an oxyuris in a lymph follicle. Sections show the worm partially or entirely buried beneath the mucosa, or there may simply remain the empty tract from which the worm has escaped. Extensive extravasation of blood, which may be interstitial or into the appendix lumen, is present. There is no infiltration of leukocytes about the parasite or his tract. One of our cases varied from this description in showing considerable necrosis and infiltration of leukocytes about an oxyuris, but bacteria were demonstrated in the necrotic tissue. Fig. 5 shows this parasite in a lymph follicle surrounded by a zone of necrosis. We have placed 6 of our cases in this group.

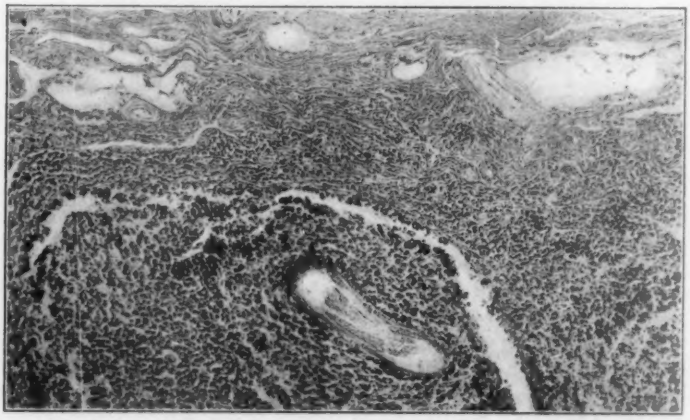

FIG. 4.—Invasion of lymph follicle by a male oxyuris. No inflammatory reaction. × 107.

3. The third group comprises cases showing destructive oxyuris lesions, for the most part hemorrhagic ulcers. There may be one or many of these ulcers in an appendix. Their size is usually small, so small in fact that they may be readily overlooked, but occasionally they reach larger dimensions. Microscopically the ulcers are characterized by hemorrhagic bases, undermined edges, and an entire absence of leukocytic infiltration about them. The base of the ulcer is usually formed by the submucosa, and is covered by a layer of necrotic material rich in red blood cells. Five of our cases showed these lesions, and have accordingly been placed in this group. In 2 of them worms were found in the ulcers.

4. In the fourth group we have placed the gangrenous appendices which have contained oxyurides. Despite long serial sections no specific lesions could be found in any of them, and they differed

in no respect, except for the presence of worms, from ordinary gangrenous appendices.

In addition to the changes described we have seen in the appendix two other phases of the oxyuris lesion. The first was encountered but once. It consisted of a hyaline oxyuris buried deep in the submucosa, surrounded by a few fibroblasts and a thick capsule of connective tissue. It is a specific healed lesion in which the host has overcome the parasite and is, so far as we know, unique. The other is a healing lesion and was also found but once. It consisted of the remains of an ulcer, surrounded by granulative tissue, and reduced to a mere slit.

FIG. 5.—Invasion of lymph follicle by a male oxyuris and secondary bacterial infection, with necrosis and dense infiltration of polymorphonuclear leukocytes. × 107.

LESIONS CAUSED BY THE TRICHOCEPHALUS. We have encountered only 2 cases of trichocephalus appendicitis, 1 catarrhal and 1 gangrenous, but definite lesions corresponding with those described by other observers were found in both of them, and they may therefore be briefly described as characteristic trichocephalus lesions. In the gross a typical trichocephalus appendix appears like an oxyuris appendix. The microscopic picture differs in that the whip-worm does not burrow so deeply as the pin-worm, but, having penetrated the mucosa, tunnels along immediately beneath it, raising it in a fold and thinning it out so that it at first appears to be an extra coat of the worm. Fig. 6 shows a trichocephalus burrowing under the columnar epithelium. The lesion is character-

istic and, like the oxyuris lesion, is entirely free from leukocytic infiltration.

The question naturally arises whether the worms produced the symptoms in the cases in which we were unable to demonstrate specific lesions. We believe that in these cases, too, they have been the exciting cause of the disease, not simply by the irritation set up as foreign bodies, although this may have been their mode of

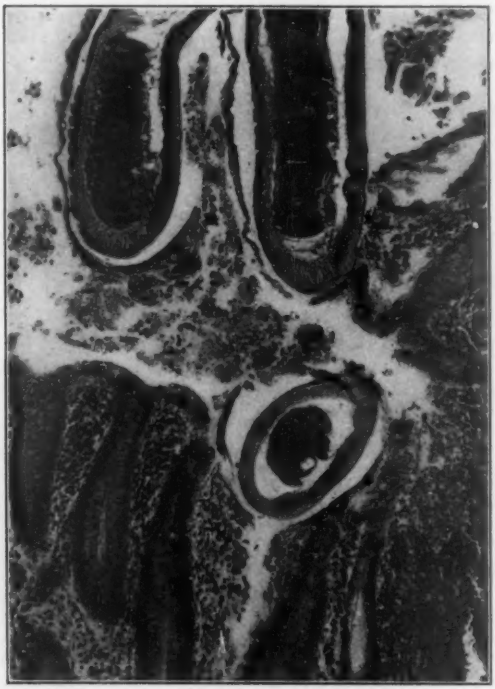

FIG. 6.—Invasion of mucosa by trichocephalus. A thin membrane of reflected epithelium is seen about part of the parasite. × 107.

action, but very probably by causing minute puncture wounds of the mucosa, which we have been unable to find. It is rather remarkable that the four appendices from adults all failed to show specific lesions. A possible explanation is that inasmuch as most of the lesions fail to produce a local inflammatory reaction, they might heal without going through the stages of repair and scar formation, thus leaving no trace of their existence behind them. In the gangrenous appendices the process may have been initiated by bacteria which gained access through parasitic lesions. Extensive

gangrene would preclude the possibility of finding specific lesions in these cases.

We have thus demonstrated in 13 out of 19 oxyuris or trichocephalus appendices, removed from children for clinical signs of appendicitis, definite lesions which we consider specific for these parasites. In 4 adult cases and in 3 autopsy cases in children no specific lesions were found.

SYMPTOMATOLOGY. In considering the symptomatology of the disease we will disregard the gangrenous cases, for in them, except possibly in respect to the previous history, the picture does not differ from that of any gangrenous appendicitis. Reference to the table shows that less than 15 per cent. belong to this variety. It is of the non-suppurative verminous appendicitis, the remaining 85 per cent., that we wish particularly to speak, for we believe that in a certain number of these cases a positive diagnosis of appendicitis due to worms can be made before operation.

In cases of appendicitis, especially in children and young adults, the patient should be questioned closely for symptoms of worms, whether they have ever been noticed in the stools, as to anal or nasal itching, capricious appetite, etc. In children the mother may give a history of the child's restless sleep, some loss of weight, or some reflex symptoms due to irritation of the genitalia. In female children there may be a vaginitis. It is surprising, however, in how few cases worms have ever been noticed by the patient or mother. The bowels may be normal, constipated, or loose. Constipation has not been particularly noted in our series. Andrikidis[2] remarks how frequently, in ordinary intestinal infestation with trichocephalus, attacks of abdominal pain with vomiting and diarrhea and a slight elevation of temperature are seen. The presence of worms or their eggs in the stools or a history of their having been previously seen is not necessarily an indication of parasitic appendicitis. We have recently had such a case in a child in which we both concurred in a diagnosis of parasitic appendicitis, but in whose appendix no worms or parasitic lesions could be found. This appendix showed catarrhal inflammation, and it is possible, as we have before mentioned, that the worm had escaped into the cecum leaving behind no visible lesion. This is in agreement with Cuthbertson, who thinks that many cases of catarrhal appendicitis with a history of only one attack are caused by intestinal parasites.

The character of the pain in parasitic appendicitis is sometimes quite distinctive. It has frequently been described as a gnawing, scratching, itching sensation in the right lower quadrant of the abdomen. In addition to this there are usually the attacks of severe pain, first localized, then general abdominal, as seen in other forms of appendicitis. Hanley's patient complained of a cramp-like, tingling sensation in the appendix. Martin and Pabeuf and Dubois[47] lay emphasis on the character of the pain, which

they say resembles the sensations caused at the anus by pinworms. Pabeuf and Dubois describe the attacks as of short duration, but in our own cases this point has not seemed particularly evident. We have noticed, however, that the pain is frequently out of all proportion to the objective symptoms and Carson thinks the attacks are characterized by an exaggeration of subjective symptoms and a comparative absence of physical signs. Pain has, in all cases, been a marked feature. The character, severity, duration, or frequency of the vomiting has not seemed to us to differ from that seen in cases of non-parasitic appendicitis, and it has been present in all but three of our cases.

On examination the patient is usually found to be a child, for the disease is essentially one of childhood and early adult life. There is frequently some anemia, but the patient, though perhaps under weight, does not, as a rule, appear very sick. The temperature has varied from normal to 103.8°, the average being about 100.5°. This does not agree with the statement of Oppe, who says there is no fever; or with the statement of Erdman that the temperature is 104° to 105° for twenty-four hours, then falls to about 99°, to be followed in a day or two by a second elevation of temperature of 1° or 2°. The pulse rate usually follows the temperature. The leukocyte count has varied from normal to 26,000 per cmm., the average being about 11,000. The polymorphonuclear cells have ranged from 42 to 87 per cent. of the total count, the average being just a little above the normal. In only a very few cases has a differential count to determine the proportion of eosinophiles been made. Where such a count has been made the percentage has been well within normal limits, except in the case of one child, aged nine years, whose appendix contained a number of oxyurides and in whose stools the ova of trichocephalus were found. The differential eosinophile count in this case was 44 per cent. This seems of interest, as trichocephalus infestation is known to give an eosinophilia while infestation with oxyuris does not.

Tenderness is, as a rule, marked on both superficial and deep pressure. In those cases which have come under our observation before operation there have been well-marked zones of cutaneous hyperesthesia corresponding to those described by Head for the appendix. Tenderness is so acute that frequently the patient voluntarily contracts the abdominal muscles, but true rigidity is so often absent that we have considered it as one of the important signs for differentiation of the disease from non-parasitic appendicitis. We have no explanation to offer for this other than that the disease is always an endo-appendicitis, with lesions confined almost exclusively to the mucosa. Carson[9] has also noted this lack of rigidity, but in most of the reports in the literature rigidity is mentioned as one of the symptoms presented by the case. We believe that if the cases were slowly and carefully examined with

this point in view, fewer cases showing rigidity would be found. There has been practically no distention in any of our cases, no paralytic ileus, and no masses. We have unfortunately not had the opportunity to examine the stools of many of our patients either before or after operation, but we agree with Metchnikoff that the examination of a single stool is, if negative, valueless. We discovered one oxyuris appendix in the early part of our study in a rather novel way. We had at first been unable to find any oxyurides in this appendix, but a few days after operation we found an oxyuris in the patient's urine, and a more careful examination of the fecal contents of the appendix disclosed oxyurides there also.

The most important points then in making a diagnosis of appendicitis due to oxyuris or trichocephalus are the age of the patient (childhood and adolescence); the history, suggestive or definite, of worm infestion; the character of the pain; the slight general constitutional reaction, and the relative exaggeration of subjective as compared with objective symptoms. There is one further suggestion in diagnosis which we would like to offer, a suggestion not original with us, but made in 1901 by Metchnikoff. In any so-called "epidemic" of appendicitis the stools of the patients should be searched for intestinal parasites or their ova. In 1896 Goluboff[25] reported an "epidemic" of appendicitis in a boarding school in Moscow, and argued that appendicitis was a specific disease, sometimes contagious. Metchnikoff in his paper aptly suggests that Goluboff might have changed his opinion if he had made careful examinations of the feces.

Prognosis. It has not been ascertained whether appendectomy in parasitic appendicitis causes a permanent disappearance of the parasites from the intestinal tract, and we have not as yet made any postoperative study of our cases on this point. Bearing in mind, however, the findings of Still, it would seem that appendectomy must in some cases relieve the intestinal tract from a constant source of reinfection.

In 43 cases of appendectomy in which the outcome of the operation was stated there were 4 deaths, or a mortality of 9 per cent.; 3 of the 4 cases were children. A study, however, of a large series of cases would probably show a mortality much less than this, for there is no apparent reason why appendectomy in parasitic appendicitis should be a more dangerous operation than appendectomy in appendicitis of bacterial origin. Indeed, the former when of the usual catarrhal type should be a safer operative case than the latter.

Treatment. Granted then that appendicitis can be caused by Oxyuris vermicularis or Trichocephalus trichiura, what is the rational treatment? Brumpt believes that medical should precede surgical treatment. Metchnikoff[41] records 3 cases, clinically

appendicitis, showing infection, with both ascaris and trichocephalus, all treated medically and all recovering. The first was a girl, aged nineteen years, who had had attacks of appendicitis for ten months. Eggs of ascaris and trichocephalus were found in the stools. Vermifuge treatment was given for four months, and at the end of that time no ova could be found. The patient was kept under observation for four and a half years and had no further attacks of appendicitis. His second case was in a child, aged twelve years, in whom the same parasites were found. This patient was relieved by vermifuge treatment and was under observation for three years without further attacks. The third case was that of a man, aged twenty-three years, who had had attacks of appendicitis for four years. His mother had died of the same disease and his sister had attacks similar to his. The feces of both the patient and his sister showed eggs of ascaris and trichocephalus. This man was treated as were the first 2 cases and was well for eight months, when he was lost sight of. In addition to these cases of Metchnikoff, Oelnitz[45] reports 21 cases of appendicitis in which trichocephalus or its ova were found in the stools. All of these cases were treated with thymol, none of them were operated upon, and all recovered and had no further attacks.

These cases suggest that there is a considerable margin of safety in the medical treatment of parasitic appendicitis. But even after finding the parasite in the stools we cannot be sure that a worm has initiated the appendicular disease; and even if we knew that a parasite were puncturing the mucosa of the appendix we could not be sure that secondary bacterial invasion had not taken place and that gangrene, perforation, and peritonitis would not be the ultimate result. Clinicians universally have long recognized the fact that the oxyuris of all the intestinal parasites is the most difficult to permanently dislodge from the intestinal tract. We have been unable to find in the literature a single case in which a person showing oxyuris or its ova in the feces and having attacks of appendicitis has been cured of his disease by medical treatment. The worm is so small that it can lodge in the appendix and presumably remain there for a long time. Especially could this be true of an appendix which was kinked or had a constriction at or near its base. As we have before stated, oxyurides are usually found in numbers in the appendix, and in practically all the cases both male and female parasites have been present. The trichocephalus, on the other hand, usually occurs singly in the appendix, although occasionally more than one parasite may be found. Girard's[24] case contained one trichocephalus of each sex. How easily then could parasites, more particularly the oxyuris, live and breed for years in an appendix, forming a constant source of reinfection to the intestinal tract, and causing from time to time attacks of appendicitis. Very little is known regarding the action

of cathartics on the appendix, and we doubt whether anything is definitely known regarding their ability to cause the appendix, normal or pathological, to completely empty itself. We cannot therefore agree with those who advocate medical treatment for cases of appendicitis in which parasites or their ova are found in the feces, for to our mind the possibility of obtaining permanent relief by this method is in the majority of cases rather remote. Appendectomy when possible seems to us the treatment of election, for by its means the individual is relieved of an ever present menace to health.

CONCLUSIONS. 1. There is a definite and characteristic form of appendicitis produced by Oxyuris vermicularis or Trichocephalus trichiura.

2. The disease is comparatively common, constituting 15 per cent. of the 129 cases of appendicitis in children, which have been the basis of the present study.

3. The typical pathological changes consist of a catarrhal type of inflammation, and punctures and ulceration of the mucosa of the appendix by the parasites.

4. The clinical picture is dominated by the exaggeration of subjective and lack of objective signs. Rigidity is frequently absent, and is almost always noticeably less than would be expected from the acute degree of tenderness present. In some instances the parasites or their ova may be demonstrated in the feces.

5. The ideal treatment is appendectomy.

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PROBLEMS IN THE TREATMENT OF EXOPHTHALMIC GOITRE.[1]

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Shortly after beginning the practice of medicine I had the opportunity of seeing and of attending, until her death, five years

[1] This paper was read in its present form before the Cooke County Medical Society, Chicago, January 31, 1912. The intention of the author to amplify it was never carried out. The paper is published, therefore, without the contemplated corrections and additions

later, a woman aged fifty-eight years, who for twenty years had been classed as "nervous" and who had, it was said, a pronounced nervous heart. The clinical picture of this individual is as clear to me today as it was thirty years ago. She was emaciated, tremulous, slightly but uniformly pigmented, with full protruding eyes and had a small, hard goitre, of which the right lobe was the larger, was subject to profuse sweats and diarrhea, had a fickle appetite and uncertain digestion, a constant tachycardia, palpitation with or without provocation, and dyspnea due to slight causes. Her disability was extreme and death, after months of cardio-vascular distress, was a welcome relief. Owing to her long period of invalidism her household was subservient to her, and about her its affairs revolved; its every thought and action depending on the possibility of weal or woe to the patient.

How many of these cases are seen, and how many years of otherwise useful activity are lost, can never be told. We know more about this condition today and to spare invalidism of this form is now considered to be the goal of both physician and surgeon, but the duty, perhaps of the former rather than the latter.

Thirty or forty years ago an invalidism of this type was attributed too frequently to nervousness, and in that convenient repository, these cases were cast and the individuals allowed to work out their own destiny without much medical aid; their comfort depending only too rarely upon the sympathy and resourcefulness of the medical advisor. Fortunate was the patient whose physician took a large view of the situation and mercifully saved the patient from the innuendoes and jibes so frequently the lot of the individual with alleged nervous disease.

The failure of the internist in the past to aid such individuals resulted in stimulating the interest of the surgeon. So active have been the efforts of the latter that in the present day it is the general belief that exophthalmic goitre is a surgical disease. It may be said without question that as long as the surgeon limited his efforts to the relief of the physical deformity associated with the disease he was acting within his domain. In many such cases, surgical intervention, aside from removing the deformity, gave a relief to the phenomenon which are now known to be due to hypersecretion of the thyroid gland. It was natural therefore, that such results, coupled with those of experimental pathology and experimental surgery, justified the surgeon in going as far as he would. That he has gone far is shown in the prevailing opinion concerning the necessity of surgical interference in this disease. This impression has gained ground because, on the one hand, of the numerous favorable results following operation, and on the other hand, because of the widely differing opinions among internists concerning the medical treatment.

Let us see whether the facts justify the position of the surgeon.

He is to be credited justly with the development of a splendid technique and with the reduction of operative mortality to a very small figure. But as to the ultimate result there remains some doubt. When we hear of a surgeon operating on a thousand or more cases and a score or more surgeons reporting their hundreds, the thoughtful observer, and especially the internist of experience, pauses to inquire: Is surgery successful because the internist has been lacking in his efforts as to general treatment? An answer to this question is difficult. One should know the course and death rate of exophthalmic goitre and of a variety of complicating conditions. These are lacking. The fact, however, remains that the problem is not the reduction of the death rate, but the prevention of invalidism, for such statistics as are available give the impression that death from exophthalmic goitre is not a frequent occurrence. The rate in medical practice is not much, if any, higher than the surgical death rate of three per cent. (this of course excludes death from mechanical causes which should never be allowed to occur). That the important problem is the avoidance of invalidism cannot be denied. In this connection, the details of the clinical histories of a few individuals, may be illustrative.

CASE I.—A woman, now aged forty-five years, was at the age of twenty desperately ill with symptoms of extreme hyperthyroidism, and for months severe nervous phenomena compelled confinement in an insane asylum; at times death seemed imminent. After a year of general medical treatment complete recovery took place. Ten years later she was still in normal condition. Four months ago hyperthyroidism in pronounced form returned, but with treatment by rest and care all symptoms disappeared. She is now suffering from pronounced myxedema. This is the third case of such swing of secretory activity from plus to minus that I have seen. Would the myxedema have developed earlier had a portion of the thyroid gland been removed early in the disease? Do we know enough of the results of present day surgical treatment of exophthalmic goitre to know that this change is not a remote possibility of operative interference?

CASE II.—When aged twenty years, Miss S. had pronounced hypertrophy of the thyroid gland with excessive secretion, characterized by such symptoms as tremor, tachycardia, nervousness, diarrhea, emaciation, and exophthalmos. After three years of continued treatment all symptoms of hypersecretion disappeared; the enlargement of the gland and exophthalmos remained. The patient has since married and has four children.

CASE III.—A business man, aged fifty years, presented, in 1897, enlargement of the gland with extraordinary symptoms of hypersecretion. A vicious life and an unusually harrassing experience in the stock exchange preceded the symptoms and the history showed a possibility of the disease having first developed at the

time of long residence in a goitre district of Michigan. The heart was very dilatable, the orifices enlarging and contracting from week to week; an aortic regurgitation appeared and disappeared. Many months of treatment were followed by a cure without return of symptoms until the present time.

Other histories might be quoted to show that it is wise to delay, or at least not to decide hastily, on the question of operation for endemic exophthalmic goitre. Many of my cases are too recent to report in final form, but my records show that with purely medical treatment a number have been cured and have remained well for six years or more.

Many minor points, it seems to me, are not infrequently ignored, or too lightly valued by advocates of surgical treatment. The latter is too frequently adopted without testing first the value of general treament. Also, it is sometimes of value to try the effect of drinking water different from that of the locality in which the patient has lived during the development of the disease, and again it is well to remember the relations, as emphasized in the earlier papers of McGraw of Detroit, which are now well nigh forgotten, of uterine and ovarian functions and of pregnancy to the secretion of the thyroid gland. My cases falling in this group are not many, but I have occasionally been impressed by the improvement of the thyroid condition after organic or functional disorders of the reproductive organs have been corrected. As an example of such improvement the following case is illustrative:

Mrs. L., five years ago, had a large fibrocystic goitre with hypersecretion and operation was necessary to avoid strangulation by mechanical pressure. Two years later the secretory symptoms returned associated with menorrhagia, and symptoms of prolapsus uteri. It was the general opinion of those who had seen the patient that it was wise to operate on the goitre and the pelvic disease at the same time. The writer believed that the latter operation would be sufficient and this alone was done; as a result all symptoms of goitre disappeared. Recently, however, after a period of a severe mental strain and anxiety the secretory symptoms recurred, but not with the same severity as before.

In a second case, Mrs. S., symptoms of marked hypersecretion of the thyroid were accompanied by a uterine disturbance, inflammatory in nature; treatment of the latter by a gynecologist led to disappearance of the pelvic trouble as well as the symptoms due to the thyroid.

After having observed many cases of exophthalmic goitre under various circumstances, the question to my mind is whether or not *any* violence to the system may not bring about temporary or even permanent relief of the symptoms. Thus, in one instance, the poor sufferer who had twice been operated on by Kocher, lost his eye by an explosion of fireworks. The eye had to be enucleated.

However, in spite of this terrible experience, the favorable progress of the thyroid condition was unaffected.

In another instance a woman aged sixty years, showed severe, symptoms of hypersecretion for five years; for two years she was in bed nearly all the time because of weakness and a bad heart. While bed-ridden appendicitis with abscess occurred, and the surgeons declined to operate. Rupture into the bowel took place and she was ill four weeks. Following this illness, such improvement in her hypersecretory phenomena occurred that she was able to walk about, and for two years she enjoyed as much relief as we often see after a thyroid operation, and as compared with her condition during the preceding two years, she was practically well. At the end of two years a bronchopneumonia developed, thyroid symptoms recurred, and recourse was had to serum, but to no avail. The question, therefore, arises, are operations on the thyroid beneficial because of the operation *per se* (White)?

The object of these remarks is to reinforce the principle, admitted by surgeons, that medical treatment, having for its object the restoration of the functions of other portions of the body is more frequently available than surgical treatment; in short goitre is not a surgical disease.

I do not make this statement to decry surgery for I have had operations performed on many individuals, as for example, those who will not or cannot take time for a long medical treatment. Indeed, I am prepared to say that with the present day knowledge which the laity possesses of the surgical treatment and with a knowledge of the uncertainity of the clinical course of the disease, it is unwise to assume the responsibility of denying surgical treatment until the patient has at least had the advantage of surgical opinion and experience. For this reason I have had many operations performed, but I am neither satisfied or dissatisfied with the results. Hence the question that ever occurs to me: Is there not more for the internist to do? There is no great amount of evidence that the surgeon himself is entirely satisfied. That surgical treatment does not obtain in the great majority of cases many surgeons admit, Charles A. Mayo endorses the statement of Kocher[2] that 90 per cent. of all goitres can be so improved by medical treatment as to make operation unnecessary. Coupled with this is the fact that Kocher has operated upon 4600 cases of goitre; in addition, in his enormous experience he has found only 780 cases of exophthalmic goitre which required surgical treatment.

These fragmentary observations, and somewhat disconnected statements, may be summarized in the following conclusions which represent the convictions of the writer:

[2] Bull's System of Surgery.

1. Endemic goitre should not be treated surgically until proper general treatment has been employed for a long period.

2. Surgical intervention should not be advised in cases of goitre associated with functional or organic disturbances of other secretory organs until the associated disorders are removed or relieved.

3. If relapse occurs in spite of general treatment, or in spite of treatment directed against the disorders of other organs, a goitre should then be treated surgically.

4. Medical treatment should be continued from six to twenty-four months. Favorable results should not be promised unless the patient is under the absolute control of a physician so that treatment by rest, diet, bathing, physical therapy, and so forth may be carried out with precision and continuity.

5. Surgical intervention requires the same rigid and prolonged after treatment to give permanent results.

Finally, my conviction is that the surgeon does too much and the internist too little in the treatment of goitre.

THYROID DISEASE COMPLICATING PREGNANCY AND PARTURITION.[1]

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In the present stage of our knowledge we recognize thyroid disease as degeneration, principally colloid in character, of the thyroid gland, resulting in deficient action and secretion, or excessive activity of the thyroid, producing an unusual quantity of thyroid secretion.

The relation between activity of the thyroid gland and functions of the genital organs in women has long been recognized. Cases of thyroid enlargement in girls at puberty frequently come under the observation of the general practitioner. Under favorable conditions the firm establishment of good general health is accompanied by the disappearance of enlargement of the thyroid.

In pregnancy, Frommer[2] has reviewed the work of Vassale in the *Italian Archives of Biology*, 1905, the *Reforma Medica*, the *Proceedings of the Medico-Chirurgical Society of Modena*, and his paper on "Tetanus," published in 1898.

By experiment and by dissection Frommer demonstrated the function of the parathyroid bodies in their production of toxins

[1] Read before the Alumni Association of the Lying-in Hospital of New York, February 13, 1912.

[2] Monats. f. Geburts. und Gynäk., 1906, Band xxiv, Heft 6.

causing eclampsia and tetany. He found these bodies small, oval, round, solid masses, 2.5 mm. to 15 mm. in diameter, yellowish red in color, and slightly harder than the lymphatics. There are two upon each side of the inner aspect of the lateral masses of the thyroid. These observations were confirmed by Humphry. In the majority of cases no colloid material was found in the parathyroids. Vassale believed that the thyroids are trophic glands, the parathyroids producing an antitoxin.

Frommer concluded that the parathyroids are epithelial organs, having an antitoxic function, whose interruption is followed by tetany, and that pregnancy and labor vitally influence the performance of their functions. When both thyroids and parathyroids are removed, fatal tetany follows. With the partial removal of the parathyroids and implantation of placental tissue, acute toxemia is produced. There is abundant clinical evidence to show from many sources that in many cases of the toxemia of pregnancy the thyroid is diseased. The administration of thyroid extract favorably influences some cases of toxemia, and assists in averting eclampsia; while in other cases the remedy produces no result. In Vassale's experience even the presence of syphilis did not prevent the favorable action of thyroid extract in the toxemia of pregnancy.

The association of pregnancy with exophthalmic goitre has long been recognized. Reviewing only the recent literature of the subject, Audebert[3] reports the case of a patient in her second pregnancy suffering from exophthalmic goitre and toxemia, although the urine contained no albumin. A milk diet produced temporary improvement, but the patient grew suddenly much worse with a very rapid pulse, and was relieved temporarily with wet cups. Coma followed, for which bleeding was done. Labor ensued, and a feeble, living child was delivered by forceps. The patient improved considerably after labor, and finally made a good recovery upon an absolutely milk diet.

The administration of thyroid extract in tablets produced no effect, but the exophthalmic goitre which had persisted for ten years completely disappeared.

Charbin[4] and Christiani report the case of a patient who had suffered for three years with myxedema and exophthalmic goitre. The extirpation of the thyroid was followed by an increase in myxedema, for which small portions of fresh thyroid gland were implanted beneath the skin, with a favorable result. A pregnancy supervened, which proceeded to a normal termination.

Potte and Kervally[5] describe an interesting autopsy upon a patient who died with eclampsia. The renal lesions were inconsiderable, and the liver was not much changed. The thyroid

[3] Annali di Ginecologia, September, 1906.
[4] Gaz. des Hôp., 1906, No. 78.
[5] L'Obstétrique, July, 1907.

gland was greatly enlarged, microscopic examination showing fatty degeneration, cystic dilatation, and the free formation of colloid material.

Fry[6] reported an excellent result from the administration of thyroid extract in a patient whose nitrogenous metabolism was greatly disturbed during pregnancy. A normal labor followed.

Gottschalk[7] describes the case of a patient suffering from a goitre so large that it caused severe pressure symptoms by interfering with the larynx and respiratory passages. The patient had never been pregnant. After the removal of the enlarged thyroid conception occurred, followed by a return of the pressure symptoms. Premature labor was induced at seven months, during which the patient suddenly died, apparently from shock.

Kron[8] reports 2 cases of exophthalmic goitre in a mild degree, which became much worse during pregnancy, and improved after labor. Kron believes that in the first half of pregnancy thyroid disease exercises a very unfavorable influence upon the embryo; but in the second half of pregnancy he considers the mother more in danger.

Lichtenstein[9] reported before the Obstetrical Society of Leipsic, a fatal case of exophthalmic goitre in a pregnant woman. The patient had passed through two pregnancies successfully, with no marked enlargement in the thyroid. A sister died of heart failure during pregnancy, another sister suffered from exophthalmic goitre. During the third pregnancy Lichtenstein's patient suffered from difficult breathing and pronounced tachycardia with exophthalmos, which developed rapidly.

On admission to the hospital her pulse was 140, the circumference of her neck, 42 cm., she was edematous, and with 2 per cent. of albumin in the urine. The uterus was gradually dilated, and without much difficulty a dead child was extracted by the breech. This was followed by a second, both fetuses being about six months advanced. The patient died in apparent collapse on the day following her delivery.

Croom[10] believes that the physiological swelling of the thyroid gland in pregnancy seldom passes to the point of exophthalmic goitre or severe disturbance. In his experience most patients who have exophthalmic goitre before conception are not made materially worse. The observation that many of the children born from these mothers are neuropathic does not, in his mind furnish an indication for the interruption of pregnancy, his view of the subject being essentially a conservative one.

Resinelli[11] reports 5 cases of exophthalmic goitre complicating

[6] Amer. Jour. Obst., October, 1907.
[7] Medicin. Klinik, 1907, No. 3.
[8] Berl. klin. Woch., 1907, Nos. 50 and 51.
[9] Zentralbl. f. Gynäk., 1908, No. 28.
[10] Edinburgh Med. Jour., 1907.
[11] La Ginecologia-Firenze, 1908, Anno 6, Fasc. 2, p. 62.

pregnancy, in all of which pregnancy produced a great increase in the severity of the disease. In 2 cases pregnancy was prolonged to its natural termination; in 2 cases labor was induced; and 1 case terminated by the spontaneous expulsion of a small and macerated fetus.

In the light of our present knowledge, Charcot's opinion that pregnancy sometimes improves these patients must be considered as erroneous. In Resinelli's experience a careful regulation of hygiene, the use of electricity, and especially the Röntgen rays, and the administration of antithyreodin are indicated; if evidence of kidney failure supervenes and the patient has reached the seventh month with a liv ng fetus, labor should be promptly induced.

Skutsch[12] reports the case of a woman, aged thirty-nine years, in her fourth pregnancy, married five years. During her first labor the thyroid gland enlarged, but afterward diminished in s ze, and in the second and third labors was not perceptibly enlarged. In her fourth pregnancy exophtha mic goitre developed rapidly; the symptoms were relieved by large doses of bromide of sodium. Nutrition failed, and during the last weeks of pregnancy the patient lost strength and became melancholic, fearing that she would die as a sister had previously died from exophthalmic goitre. Labor developed spontaneously with the expulsion of dead twins, at about six months' development. There was little hemorrhage, but on the following day, after great restlessness and coma, the patient died.

Skutsch cannot believe that pregnancy in itself causes exophthalmic goitre. He believes that individual cases vary greatly as to the development of dangerous symptoms. There can be no question, however, but that the disturbance in metabolism caused by pregnancy is very dangerous to a patient having exophthalmic goitre, or having a predisposition to it. He considers the great disturbance in the action of the heart as especially dangerous. He positively denies the opinions previously advanced by Charcot, Carlein, Trousseau, and Sonza-Leibe, that pregnancy ever influences exophthalmic goitre favorably.

Massini,[13] of Buenos Ayres, has studied the influence of thyroid conditions upon eclamptic convulsions. His experiments show that while three-fourths of the gland may be safely extirpated in non-pregnant bitches, in pregnant bitches the same operation is followed by severe convulsions.

Ward[14] reviews extensively the literature of thyroid disease and reports fully the interesting case of a primipara at the end of the third month, married six years; two miscarriages, spontaneous

[12] Zentralbl. f. Gynäk., 1908, Band lxviii, p. 917.
[13] Paper published in Spanish and reprinted in L'Obstétrique, 1908, No. 5.
[14] Surg., Gyn., and Obst., December, 1909.

at the third and fourth weeks. The family history showed exophthalmic goitre. The patient, when aged twelve years, had nervous symptoms of the disease manifested later on by tachycardia. This was improved by the use of cytotoxic serum and thyreoglobulin. Curetting was performed. This was followed by a marked return of the symptoms, which subsided under the serum treatment. Pregnancy ensued. The patient was decidedly nervous and restless, with moderate hypertrophy of the thyroid, constipation, and morning sickness. Injections of thyreoglobulin appeared to be beneficial until the end of the fifth month, when the urine greatly diminished, headache and vomiting becoming severe. In the sixth month a nitrogenous partition showed ammonia, creatinin, and rest nitrogen, greatly increased, with diminished urea. During the first two weeks of the sixth month the dose of thyreoglobulin was increased to 10 minims, twice daily; then three times daily, acting almost as a specific. The urine increased following the injections. During the seventh month the patient was very ill, with exhaustion and greatly diminished nitrogenous excretion. In the eighth month it was thought impossible for the pregnancy to proceed, and labor was induced by manual dilatation and bags. Dilatation being difficult, vaginal hysterotomy was performed, and a feeble child, weighing 6 pounds, was readily delivered by forceps. The placenta was adherent and was extracted. The patient rapidly recovered. The child lived thirty-six hours, dying from intracranial hemorrhage.

Ward calls attention to the use of a saline extract of thyroid proteids made from fresh normal human glands as being more efficient than sheep thyroids, as ordinarily prepared. The hypodermic method he considers much superior to administration by the mouth.

Seitz[15] reviews previous experiments upon the relation between disease of the parathyroid bodies and eclampsia. His studies led him to conclude that during pregnancy the parathyroids become softened, more vascular, with an increase in the chromophile cells. In eclampsia these cells are lessened or disappear. Connective tissue increases, fatty colloid material and cysts develop. In some cases tuberculous infection has also been present. He believes that one must sharply distinguish between tetany in pregnant animals produced by partial or total removal of the parathyroids, and eclampsia. The so-called eclampsia of animals as seen in the cow he considers tetany and not true eclampsia. Nor does he believe that extract of the parathyroids can be successfully used in eclampsia.

Stowe[16] brings an interesting point into the study of this subject in reporting the case of a young woman in her second pregnancy, who a year previously had an abdominal section for acute appendi-

[15] Arch. f. Gynäk., 1909, Band lxxxix, Heft 1. [16] Amer. Jour. Obst., May, 1909.

citis, at which miliary tuberculosis of the peritoneum was also found. She had an abortion caused by exophthalmic goitre which developed rapidly just before the abortion; and after abortion she suffered from slight exophthalmos, nervousness, tremor, rapid heart action, increased reflexes, and enlargement of the thyroid. This condition was somewhat improved by rest in bed, the application of ice, and the use of sedatives. When the second pregnancy occurred her symptoms became worse, vomiting developed, and the patient grew very rapidly ill, with diarrhea and bloody discharges. The urine contained 2 per cent. of albumin. The uterus was emptied by rapid dilatation, under ether, and during the next three days the vomiting ceased, the diarrhea diminished, but the patient was delirious, with incontinence of the bladder and bowels. Icterus, petechiæ, and enlargement of the liver developed, with active restlessness and twitching of the limbs, without convulsions. Death ensued, and an autopsy could not be obtained.

Bonnaire[17] reports the case of a primipara in the seventh month, who had very rapid swelling of the thyroid, syncope, and paralysis of the right vocal cord. There was no exophthalmos or tachycardia. Labor was induced by introducing Tarnier's bag into the cervix. This was followed by improvement in the respiration, although labor did not develop, and the bag was removed. During the last two months of pregnancy the patient had frequent attacks of hysteria, which were ascribed to the thyroid autointoxication.

A second case was that of a patient in her second pregnancy who had great enlargement of the thyroid, which disappeared very largely after her confinement. In the third pregnancy the thyroid again enlarged, the right being much more swollen than the left half. Exophthalmos and dilatation of the heart, with disturbed circulation developed. There was also edema of the lungs, diarrhea, 4 per cent. of albumin in the urine, cyanosis, and dyspnea. An attack of syncope was followed by the patient's transfer to the hospital, when another attack so severe as to threaten her life occurred. Free bleeding improved the condition somewhat, and labor was introduced by the introduction of a bag. A living child, ill-developed and under weight, was born. The patient apparently improved, but two hours after labor she had a severe postpartum hemorrhage and collapse, from which she slowly recovered. The exophthalmic goitre remained, although less severe.

Goodall and Conn[18] contribute a very interesting paper upon the relation of the thyroid gland to the female generative organs. They cite the case of a patient who had passed the menopause,

[17] Presse Médicale, 1910, No. 28.

[18] Surg., Gyn., Obst., May, 1911.

after normal childbirth. She lost weight, and suffered from dull, aching pain in the lower abdomen. The neck enlarged, with dyspnea, and dysphagia.

On section, chronic pelvic tuberculosis was found, the tubes were dilated with pus, the ovaries were riddled with abscesses, dense adhesions, and one pus tube communicated with the bowel in two places. The uterus and appendages were removed, the bowel closed, and the abdominal cavity drained through the vagina. Recovery was complicated by abscess, with a discharge of pus through the abdominal incision. The thyroid gland steadily decreased in size and became much smaller than normal.

Goodall and Conn have found no similar case reported in the literature. They report a case where amenorrhea was greatly improved by the administration of thyroid extract, and another where amenorrhea and epilepsy, without apparent thyroid change, were greatly improved by thyroid extract. Sterility, obesity, and menorrhagia, have also been improved in their observation by thyroid extract. In another patient hysterectomy, with the removal of the right tube and ovary, was performed for excessive hemorrhage from the uterus, with symptoms of myxedema. This patient was greatly improved after operation by the combined administration of calcium lactate and thyroid extract.

These cases are cited as those in which deficient action of the thyroid has produced disturbance in the functions of the generative organs. The case of tuberculosis complicated by thyroid disease is apparently unique. Pinard's cases of disturbed menstruation from thyroid disease are quoted.

They conclude that the relation between the female genitals and the thyroid is very intimate, and that the thyroid and ovaries mutually influence functional activity. Thyroid secretion and ovarian secretion neutralize each other, the secretion from the interstitial cells of the ovary apparently bringing the ovary and thyroid into close relation. Ovarian hyperactivity is a frequent cause of the development of exophthalmic goitre.

Porter[19] reports 2 cases of hyperthyroidism in women, one of which was relieved by the administration of thyroid extract, the other by injections of boiling water into the thyroid gland. He also reports the case of a patient in labor with her fourth child, with marginal placenta prævia. On admission to the hospital the cervix and vagina were tamponed with gauze, which controlled the hemorrhage. At the end of five hours the patient became very restless, with rapid and irregular pulse. She was immediately delivered under ether of a small, poorly nourished, dead child. There was not sufficient uterine hemorrhage to account for the symptoms. On the following day she suddenly developed a very rapid, weak pulse, with air hunger.

[19] Amer. Jour. Obst., 1911, No. 5.

On examination a medium enlargement of the thyroid gland was found, and it was ascertained that during her pregnancy the patient had suffered from frequent attacks of tachycardia. Porter reports other cases illustrating the general effect of thyroid disease, and in another paper,[20] gives the results of his treatment of hyperthyroidism by injecting boiling water into the gland. This treatment stops the excessive activity of the gland, and may give the patient an opportunity to recover sufficiently to have the gland safely removed by a surgical procedure.

In my experience it is no unusual thing to observe disturbance of the functions of the genital organs in women, associated with varying degrees of thyroid disease. At the Jefferson Maternity we have several times observed patients with enlarged thyroids who passed through labor with little disturbance, without much increase in the thyroid, with moderately well-developed children, and who made fairly good recoveries.

Among my private cases within the last few years it has been my fortune to see 4 patients in whom thyroid disease, with or without other complications, proved a critical factor in determining the life of mother and child.

Case I.—A tall, pale, brunette. During her first pregnancy her family physician thought she had diabetes, because she had edema and sugar in the urine. Patient denied enlargement of the thyroid gland at that time. She gave birth to a healthy, male child, which she nursed thirteen months.

The first pregnancy terminated prematurely at about the eighth month. In the second pregnancy no enlargement of the thyroid was observed when the patient first came for examination. The pulse was normal, the tongue slightly furred and coated, and the patient pale. The pelvis was normal. Aside from her pallor and unusually nervous condition she presented no abnormality. An examination of the urine was negative. Spontaneous labor developed rapidly, with great excitement, the mother becoming unmanageable. Amniotic liquid was in excess. The child weighed 7 pounds and 3 ounces, and was fairly nourished. The placenta contained infarcts along its edges. The patient had an excessive secretion of milk, and nursed the child, but remained in a highly neurotic and hysterical condition. Involution proceeded fairly well, retroversion developed, the uterus being readily replaced in the knee-chest posture. At birth very slight lacerations in the anterior and posterior segments occurred, which were immediately repaired, and healed completely.

Ten months afterward the patient presented herself in wretched health. Bilateral goitre had developed with exophthalmos of moderate degree. The pulse was 130. The patient was highly

[20] Jour. Amer. Med. Assoc., September 30, 1911.

excitable, complaining of pressure symptoms and difficulty in breathing. She first noticed this condition five months after the birth of her child. She ascribed her bad feelings to a slight protrusion of the anterior vaginal wall, which she had noticed, and over which she became excessively anxious. She was urged to submit to surgical treatment for the goitre, but declined, and went to a physician, who gave her iodine. Three months later she was worse, suffering from frequent diarrhea, with headache and backache, and still possessed with the belief that her symptoms depended entirely upon the cystocele. A ring pessary readily replaced the vaginal wall. A month later she was slightly better, but would submit to no operation for the relief of the cystocele.

She passed from observation at this time. Five months later, or eighteen months after her last pregnancy, she submitted to operation at the hands of another physician for prolapse of the vaginal wall. This operation was followed by unconsciousness and delirium, in which she died. An autopsy could not be obtained. A sister also has goitre.

The significant facts in this case were the insidious development of the disease, apparently induced by two pregnancies, the first terminating prematurely after the patient had had sugar in the urine, with edema. The second pregnancy was characterized by excessive nervousness, increased amniotic liquid, slightly diminished development of the child, great excitement during labor, with hypersecretion of milk. Obstinate constipation was a factor which caused the patient to strain, and which produced the downward displacement of the vaginal wall. During the latter months of her life the patient's condition was practically that of hysteromania.

Case II.—Patient slender, fairly nourished, blonde, the wife of a professor in a college for women, and herself an instructor and lecturer on philosophy. Her early general health was good. Her first pregnancy terminated in a very prolonged and difficult labor, during which the physician in attendance considered the question of Cesarean section.

The patient first came for examination to have the presence of a pelvic deformity determined. On examination she was found to have a narrowed and flattened pelvis, with an external conjugate of $18\frac{1}{2}$ cm. The symphysis was unusually high and the vaginal tissues normal. The patient was informed that should a second pregnancy occur the life of the child would be best guarded by elective section. When pregnancy supervened the patient did well in the early months, but gradually began to suffer from nausea, exhaustion, and headache. There was slight enlargement of the thyroid, which dated from the first pregnancy, and had never disappeared. The urine showed deficient nitrogenous metabolism. The patient's condition was somewhat improved by the use of

thyroid extract and rest, the nitrogenous metabolism growing no worse. The thyroid extract was continued, with occasional intermissions, throughout the pregnancy in very moderate doses. The central lobe of the thyroid became as large as a small orange. Her general condition remained good.

The patient was allowed to go to term, when regular labor pains began, with attacks of great nervousness. She had entered the hospital a few days previously, and section was immediately performed, with the delivery of a male child, weighing between 6 and 7 pounds. During the first twenty-four hours after operation the patient was restless and exceedingly nervous. Hardened feces and fecal sand were discharged after the operation. The secretion of milk gradually formed, and the patient was able to nurse the child for some time. Six months after delivery the thyroid had increased distinctly in size. The general health was fairly good, and the patient was still nursing the child most of the time. She was advised to gradually wean the child, and enter the hospital again for the removal of the thyroid. Thyroidectomy was performed at the Jefferson Hospital by Dr. Gibbon, leaving a portion of the capsule to avoid the bad results of total removal. The patient's recovery was uncomplicated.

Eighteen months after the delivery of the child the patient was in excellent health. She was slightly thinner, but able to resume her duties as a teacher, was free from the fainting attacks which had previously annoyed her, and considered herself in excellent health. Her child had done well.

CASE III.—A multipara was brought to my attention by her sister, a trained nurse. The patient was seen at her home, giving the following history: Enlarged thyroid in the family; her parents, although having it, are living and in good health. Patient aged between thirty and forty years, moderately stout, and apparently fairly nourished. Usual diseases of childhood; mild attack of scarlatina. Menstruation began when aged between twelve and thirteen years, varying from twenty-eight days to five weeks. From twenty to twenty-three years of age she suffered considerable pain; between the ages of thirteen and fifteen years she had attacks called congestion of the brain, with headache and unconsciousness for several hours. Married twelve and one-half years, the present being her seventh pregnancy. The first pregnancy terminated in abortion at seven weeks, preceded by pernicious nausea. The second pregnancy was associated with pronounced nausea, with abortion at six weeks, said to be produced by overexertion. In the third pregnancy, severe nausea, pregnancy terminating at seven and one-half months, the child living nineteen days, and dying with jaundice. The fourth pregnancy went to four weeks, when the patient had a violent cough which she thinks produced abortion. In the fifth pregnancy she had pernicious

nausea for five months, but went on to term, and was delivered in the hospital by the application of high forceps. She was delivered of a female child weighing 7½ pounds, which died twelve hours after birth from birth pressure.

By examination of the patient the case was probably one of posterior rotation of the occiput. She was considerably torn, and had stitches placed in the perineum and the pelvic floor. The sixth pregnancy terminated at about the normal term, with spontaneous labor, the child being a male, weighing 8 pounds. It was allowed to nurse the mother. The child did not discharge the contents of the bowel freely, and died in twelve days, with jaundice and intestinal disorder.

The present seventh pregnancy, was characterized by nausea, which was constant, with not much vomiting. In each pregnancy the thyroid had enlarged very much, and at the time of labor had become greatly distended and occasioned pressure symptoms. When examined the patient had frontal and right-sided headache, gas in the intestine, backache, and at times swelling of the limbs. The bowels moved sluggishly. The thyroid gland was larger than it had ever been, and twice in the patient's history this enlargement had been accompanied by a marked nervous disturbance.

On examination, the right lobe of the thyroid was markedly enlarged, the neck measuring 16½ inches in circumference. The pulse was about 90, irregular, with great variations in tension. There were no heart murmurs, nor could enlargement of the heart be detected. The head and eyes were apparently normal, the tongue broad, thick, fairly clean, and flabby. Liver dulness extended one finger's breadth below the ribs. The abdomen was tympanitic; the fundus of the uterus could not be distinctly outlined by palpation; the pelvis was of ample size and its contour fairly symmetrical. The pubes were slightly higher than normal, and the pubic arch was more narrow than normal.

On vaginal examination the promontory of the sacrum could not be reached without excessive and painful pressure. The uterus was enlarged, the lower uterine segment present, and the period of gestation about three months. The position of the uterus was normal, and there was no evidence of pelvic disease. On the right side the cervix was torn to the vaginal junction, and the pelvic floor relaxed.

The patient had been under the care of a local physician who had made examinations of the urine, reporting no casts, and no albumin. The nitrogen partition of the urine in a specimen sent three weeks before the patient was seen showed: Reaction alkaline, turbid, straw colored, specific gravity, 1016, no serum or nucleoalbumin, no mucin, urea, 1.2 per cent., no casts, a few uric acid crystals, a few squamous epithelial cells. The amount in twenty-

four hours was 1700 c.c.; the total nitrogen was 11.90 grams, of which the urea nitrogen was 55 per cent., the ammonia nitrogen, 23.9 per cent., the uric acid and purin nitrogen, 1.2 per cent., creatinin and rest nitrogen, 19.9 per cent. Another specimen examined before the patient was seen showed 2350 c.c. in twenty-four hours, with a total nitrogen of 17.10 grams, of which the urea was 71.3 per cent., ammonia 11.5 per cent., uric acid and purin, 1.1 per cent., creatinin and rest nitrogen, 16.1 per cent.

A diagnosis was made of toxemia accompanied by pathological changes in the thyroid. The patient and her husband were very desirous of obtaining a living child. They were advised to put the patient under treatment, at rest, owing to the toxemic and thyroid condition, to avoid labor by elective section, as the thyroid had so enlarged at labor as to cause the patient intense suffering and to interfere with the mechanism of labor through her prostration; and when convalescent to submit to the surgical removal of the greater portion of the enlarged gland. This advice was taken, and the patient allowed to remain in her home in Ohio until the child was viable, at twenty-six weeks' gestation. She was placed upon a milk and vegetable diet, with the persistent use of thyroid extract in varying doses. Twenty-four-hour specimens of urine were sent for nitrogen partition at regular intervals. These examinations showed a gradual improvement by increase in the urea nitrogen, and diminution in the ammonia nitrogen, although the creatinin and rest nitrogen remained above normal. The patient was much encouraged by her physical improvement and very hopeful. Her pulse ranged from 104 to 108, blood pressure, 130 to 160 mm. She was able to take exercise with little respiratory disturbance. Nausea and headache disappeared; appetite and sleep improved; and the bowels moved regularly. The movements of the child became evident. The patient went on to gradual improvement, the nitrogen partition demonstrating the improved metabolism until she reached, as nearly as could be estimated, twenty-six or twenty-seven weeks of gestation. She then came to Philadelphia so that the child could be delivered, if necessary, at any time.

On examination, she was then looking well, pulse, 110 to 112, with variable but nearly normal tension. She followed strictly the diet ordered, and took one grain of thyroid extract three times daily. The thyroid was evidently larger than when first seen, but did not cause difficulty in breathing, and upon palpation, was evidently cystic. There was no edema, and fetal heart sounds were plainly heard on the left side anteriorly. The patient went on until the ninth month, when it was found that the neck had enlarged half an inch in two months. Fluid appeared in the breasts, and the head of the child descended slightly into the upper pelvis. At about two hundred and sixty-five days, as nearly as could

be ascertained, the patient entered the Jefferson Hospital, because she had been in a highly nervous and sleepless condition for several days. Edema had appeared in the lower extremities, and the patient had lost appetite and was much disturbed.

Operation was performed as soon as practicable, and a well-developed male child, weighing 8 pounds and 13 ounces, in breech presentation, was delivered by celiohysterotomy. The operation proceeded smoothly, being complete in thirty-seven minutes. The patient endured anesthesia well, without much dyspnea. She reacted well, and was very nervous and excitable during the night following the operation. The child had abundant secretion of mucus in the nose and throat, but no cyanosis, and seemed to do well. Mother and child progressed favorably after the operation. The child was not allowed to nurse, but was artificially fed, and received daily copious irrigation of the intestine, with small doses of brandy and water. For the first few days it lost considerably in weight and had abundant movements of greenish mucus. This gradually gave way to normal movements under a carefully selected milk feeding. The mother had no milk in the breasts, and at times was in a highly nervous condition. Her recovery was complicated by a stitch abscess in the lower portion of the abdominal incision, and the breaking down of subcutaneous fat. Mother and child left the hospital in good condition a month after the operation, the child weighing 10 pounds and 3 ounces. The child has steadily improved and is exceptionally vigorous and well developed.

The stitch infection of the subcutaneous tissue made its way downward to the peritoneum and infected one of the uterine stitches, the uterus evidently being adherent to the abdominal wall. Several silk stitches were passed through a small abdominal fistula, which finally closed. The mother did well after the operation for three months, when the thyroid gland became larger, and she became highly nervous and apprehensive, with loss of appetite. Menstruation had occurred twice, with considerable flow. There was no pain or distress, and the patient was able to take whatever exercise she desired.

During the last summer the patient consulted Dr. Charles Mayo, at Rochester, Minnesota, where the right lobe and isthmus of the thyroid were enucleated. It was found to be in a highly colloid and cystic condition. Following this the patient's general health has gradually improved. Her child is exceptionally vigorous and well nourished.

Delivery by elective Cesarean section before labor pains develop was selected in this case to avoid the enlargement of the thyroid, which had occurred at previous labors. This enlargement had been so great as to cause severe pressure symptoms, and to interfere with the normal action of the uterus and indirectly with the

mechanism of normal labor. Elective section was selected in the interest of the child, to avoid abnormal mechanism in labor, and the delivery of the child in an unfavorable position and presentation, through a partly dilated birth canal.

Case IV.—Primipara, seen in consultation seven years previously. Mother had pelvic tumor and asthma. Sister in average health. The patient had suffered from pelvic pain and had abdominal section, with the removal of the greater portion of cystic ovaries and shortening of the round ligaments. Married for several years. She had despaired of having a child, and had adopted one. Shortly after menstruation ceased, and the patient had nausea, headache, edema, and albumin in the urine. There had been a bloody vaginal discharge at intervals.

On examination, the patient was between seven and eight months pregnant, no evidence of placenta prævia could be found, and the fetus was living. The mother's heart beat strongly and the pulse irregularly without much tension. The patient was unable to assimilate much food; the thyroid gland was not enlarged, but the patient was evidently toxemic. Five days afterward she expelled a premature female child, weighing $2\frac{3}{4}$ pounds. The child lived forty-eight hours, having frequent attacks of cyanosis, and dying on the third day after birth.

Three years afterward the patient again came under observation, stating that since her first labor she had suffered from headache, nervous exhaustion, and astigmatism, for which glasses gave little relief. She had lost in weight. She was then four months pregnant, having bloody vaginal discharge at intervals, with polyuria, passing on one occasion 142 ounces in twenty-four hours. The bladder was very irritable, and nausea was almost constant. The patient slept poorly and was very constipated. She had attacks of jaundice, and had felt fetal life.

On examination, the pulse was rapid, with high tension. Examination of the blood showed hemoglobin, 50 per cent.; leukocytes, 6600; red cells, 3,755,000. No enlargement of the liver could be detected. There were no maternal heart murmurs. Examination of a twenty-four-hour specimen of urine showed: Acid reaction, specific gravity, 1006; pale, straw colored, turbid; no serum albumin, no sugar, no casts, and amorphous urates. The urea nitrogen was 73.3 per cent.; ammonia, 8.2 per cent.; uric acid, 8.5 per cent.; creatinin and rest nitrogen, 10 per cent.

The patient was placed upon a restricted diet, with a bitter and arsenical tonic, under which her condition temporarily improved. Thyroid extract, 1 grain, three times daily, was added. This treatment was continued, with little variation, for three months, the patient doing fairly well.

Labor was spontaneous, with the birth of a male child, weighing between 7 and 8 pounds. The patient was anxious to nurse

the child, and had considerable secretion of milk, which agreed with the infant. During lactation the patient had several attacks of engorgement of the breasts, with rise of pulse and temperature, and with some disturbance in the bowel movements of the child. The use of calomel, thyroid extract, and hot baths gave relief. Three months after delivery the pelvic organs were normal, the tongue clean, the breasts normal, and the patient in good general condition. The child was gradually weaned at seven months and became vigorous and fairly well developed.

During pregnancy and the puerperal state no gross alterations in the thyroid gland could be detected. The benefit following the administration of thyroid extract in the condition of mother and child was evident.

The child suffered from attacks of intermittent toxemia, which were controlled by a milk diet. The mother continued in good average health.

In this case the administration of thyroid was followed by immediate improvement in the nitrogenous metabolism, and apparently influenced favorably the secretion of milk.

The mother, who was formerly a nurse, ascribed her successful pregnancy to the prolonged use of thyroid extract.

In my experience, in examining all cases of pregnancy, the condition of the thyroid gland should receive attention. If this be manifestly enlarged or altered the patient's nitrogenous metabolism should be closely watched, and if evidences of lack of thyroid secretion be found, the active principle of the glands in some available form should be administered. I have seen the best results by small doses, 1 grain three times a day, continued for from four to seven months.

Our most reliable methods of ascertaining the patient's condition are nitrogen partition of the urine and the clinical study of the condition of the circulation. Unfortunately, pulse tension varies so greatly, sometimes under the excitement of examination, that it is not as constant and reliable a factor in diagnosis as we have hoped and wished. The nitrogen partition, in our experience, is much more reliable.

The wishes of the parents should be carefully ascertained regarding the life of the child, and the situation clearly explained to them. Where children have been lost in previous pregnancies, and the parents are desirous of offspring, all possible means should be used to continue the pregnancy, without undue risk to the mother. If there is a history of enlargement of the thyroid during labor, with the development of unfavorable mechanism and loss of the child through birth pressure, elective Cesarean section before labor should be selected.

No case should be considered as convalescent, or receiving adequate attention, in which the patient after recovery from

parturition does not seek surgical advice and treatment to permanently remedy the thyroid condition.

The induction of labor in these cases is seldom indicated as it is too slow and uncertain. The pressure of elastic bags increases the mother's nervous disturbance, and delivery of the child through a partially dilated birth canal exposes it to additional risk.

In cases where degeneration of the thyroid gland does not seem to be present, but an increased secretion of thyroid material is formed, absolute rest and milk diet, sedatives, and the application of ice over the gland, should be immediately employed, with the hope of improvement until the child can become viable. As reported cases show, it is sometimes possible to check the thyroid activity by this means, and to bring the patient to a safe and spontaneous termination of pregnancy.

FUNCTIONAL TESTS FOR HEPATIC CIRRHOSIS.

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In its advanced state, cirrhosis of the liver is one of the less difficult conditions to recognize; but this can hardly be said of the incipient stages of the disease. One is not infrequently tempted to hazard a diagnosis of cirrhosis in those individuals described by Frerichs, "Who devote themselves too freely to the pleasures of the table and who make use of a succulent, stimulating diet, notwithstanding their sedentary mode of life;" but in the absence of physical signs opinion can amount to little better than conjecture. It is in response to a demand then that the various functional tests have been advanced, and it is the object of this paper to discuss the more important tests and their limitations.

If the present trend of ideas in physiology is in any degree correct, the liver is peculiar in the number and variety of functions that it fulfils, and these are not only secretory and excretory, but are also related to many of the finer chemical processes of metabolism, as, for example, the glycogenic and the cleavage of amino-acids. All of these activities are essentially enzymatic, and consequently it is to be inferred that any morbid process influencing the hepatic cellular nutrition would as a direct result have some bearing upon the fate of those bodies normally acted upon in the liver. The only exception logically, would be in case of hepatic functions being vicariously performed by some other organ when the liver is incapacitated through disease.

On account of the bile production appearing peculiar to the liver it was at first assumed that urobilin, because of its close chemical relationship with bile pigments, depended exclusively on the hepatic cells for its formation. A closer study of the subject, however, has shown that several other factors are to be considered; the most important, perhaps, being the reducing action of the intestinal bacteria on the bile pigments.[1] It is not definite whether the liver of itself can produce urobilin from its precursor bilirubin, or whether the former substance results only from bacterial reduction. The question must be left open for the present. Any diagnostic interpretation, therefore, put upon urobilinuria in the present state of our knowledge must be empirical rather than founded upon definite and demonstrated facts. Urobilin may be found in excess in the urine, associated not only with cirrhosis of the liver, but also with passive congestion of cardiac origin and infections involving the liver parenchyma generally.[2] The fact that urobilin may be increased in the urine in some diseases other than those of the liver, for example pernicious anemia, does not of necessity vitiate its value in diagnosis, since interpretation can be made in the light of other diagnostic data. The presence of excessive amounts of urobilin may be given some consideration while its absence would be ignored in the face of other evidence. In Germany particularly a certain confidence is placed in the significance of this body that is not universally felt, at least not in America. Fischler, for example, makes use of the urobilin test in estimating the degree of compensation attained by a discompensated heart. It is claimed that grades of congestion which are not to be detected in enlargement of the liver are nevertheless evidenced in a disturbed hepatic function and that urobilinuria is an expression of such an impaired activity. Fischler's observations are capable of being interpreted in another way, however, for while it may be true that passive congestion too mild to induce an increase in liver volume may impair hepatic function, it is not to be overlooked that in broken compensation there is an increased blood destruction[3] and the pigments arising therefrom might also give origin to an increased urobilin excretion. Whenever there is an abnormal breaking down of the red cells of the blood, as is the case with some infections, there appears to be an increase in the formation of urobilin, which fact in some degree, at least, complicates the problem of the relation of urobilin to hepatic cirrhosis.

The urine was tested for urobilin by means of the regular tests, including the spectroscope, in all of the cases of cirrhosis mentioned

[1] Muller, Verhand. d. Schles. Gesell. f. vaterl. Kultur., January, 1892.

[2] Fischler, Münch. med. Woch., 1908, lv, pp. 1421–27; Verhand. d. Kong. f. inn. Med., Wien, 1908, pp. 445–50; Deut. Arch. f. klin. Med., 1908, xciii, p. 427; Arnsperger, Beitr. z. Chir., 1906, lii, p. 46: xlviii, p 725.

[3] Grawitz, Klin. Path. des Blutes. 1902, S. 491.

in this paper, and was found present at least once in 65 per cent. of these cases. The same tests were applied to 50 urines from patients who complained of various forms of mild digestive disturbances where there was no ground to suspect liver disease in an anatomical sense, although a physiological derangement could not be excluded. In 26 instances urobilin was present (52 per cent.). It was also found in 31 of 100 urines from miscellaneous cases of various diseases of all sorts. Cases suspected of hepatic disease were excluded from this last series. In view of these results it seems conservative to assert that no reliance can be placed upon the test when one is in a diagnostic dilemma.

In this connection mention may also be made of the aldehyde reaction of Ehrlich. For some time this reaction was supposed to be due to urobilin,[4] but it has been pretty well demonstrated by Neubauer[5] that it is the pyrrol radicle present in urobilin that produces the color effect. While urobilin does give a rose color with the aldehyde reagent other substances which may occur in urine produce the same result. I have employed this test among others, and while there is often agreement between the aldehyde and spectroscope[6] tests, it is not invariably so, and on that account it seems most probable that several substances in the urine can effect this reaction.

In 1901 Strauss[7] published a functional test for hepatic insufficiency which depends on the theory that glycogenesis of levulose is exclusively confined to the liver cells. Since the first communication this test has been extensively employed, especially in Germany, and has earned a certain respect among clinical procedures. The method of use of the levulose test, as is well known, is to give to the fasting patient, preferably before breakfast, 100 grams of levulose, dissolved in either water or tea. The urine is collected for several hours after the levulose is taken and tested for the presence of that sugar. The presence of an alimentary levulosuria is considered indicative of hepatic insufficiency. In a summary of the literature, Chajes[8] found this test positive in 86.9 per cent. of the cases of clinical cirrhosis. The defect in this procedure lies not in that all cases of cirrhosis do not respond with levulosuria, but in the fact that a considerable percentage of normal individuals respond as well. Churchman[9] has emphasized this point in a recent communication. He found that 9 of 38 cases, liver normal clinically, gave a positive test (23.6 per cent.), and Frey[10] estimates from his experience that 10 per cent. of normal persons would give a positive test and 50 per cent. of the cases of hepatic cirrhosis.

[4] Hildebrandt, Zeit. f. klin. Med., 1906, lix, pp. 351–441.
[5] Zentralbl f. Physiol., xix, p. 145; Verh. Deutsch. Natur-forschr. u. Aerzte, 1903, ii, p. 68.
[6] For quantitative methods consult Hoppe-Seyler, Virchow's Arch., 124
[7] Deutsch. med. Woch., 1901, No. 44, p. 757.
[8] Ibid., 1904, xxx, p. 696.
[9] Johns Hopkins Bulletin, 1912, xxiii, p. 10.
[10] Zeit. f. klin. Med. 1911, lxxii, pp. 383, 436.

Ten normal persons and 20 cases of cirrhosis were used in estimating the value of the Strauss test. The technique differed in no respect from that usually employed. Of the 10 normal individuals 3 responded with levulosuria (30 per cent.). It is of interest that one of these, a young man, who was induced to take the levulose a second time had no sugar in his urine on the second test. The cases of hepatic cirrhosis selected were all of an advanced type, with ascites, and were regarded as typical cases. The levulose in several instances was given two or more times. Fourteen of these cases responded with levulose in the urine (70 per cent.). Levulose was also given to a number of patients not regarded as having hepatic disease. One of these was a typical case of Charcot's hepatic fever; the Strauss test was positive, although at the time of operation (gallstones) the liver appeared normal. A young man with chronic adhesive pericarditis and enlarged liver gave a negative test, but two days later a second test was clearly positive.

In a recent communication Pari[11] concludes that the assimilation for galactose is so inconstant that clinical deductions in cirrhosis of the liver are very uncertain.

An attempt was made to put the whole matter of sugar tolerance in its relation to liver function on a more stable basis by resorting to animal experimentation. If the liver is indispensable for the rapid removal of absorbed sugar from the blood stream, then in dogs with Eck fistulas there should be an easily induced alimentary glycosuria. Normal dogs are capable of withstanding 10 grams of glucose per kilo of body weight without mellaturia. The tolerance for levulose was found a little higher than that for glucose. Now after an anastomosis between the portal vein and the inferior vena cava the liver no longer acts as a screen between the area of absorption and the systemic circulation (kidneys). It was observed[12] that the sugar tolerance for both glucose and levulose falls after this operation but, briefly, that levulose is better cared for than glucose. This would suggest that so far as levulose is concerned it is less dependent on perfect hepatic activity than glucose. There was also noted a remarkable fluctuation from day to day in the ability to utilize sugar as measured by the amount recovered in the urine. This bore some relation to the state of nutrition of the animal. Dogs with Eck fistulas are difficult to feed, and inevitably become undernourished after a period; and it was noted that in the later experiments, when presumably the glycogen stores of the organism were depleted, the tolerance for sugars was highest. This fact may be the explanation of some of the clinical observations.

The relation that the liver holds to nitrogenous metabolism is

[11] Gazz. degli Osped. e degli Clin., 1912, xxxiii, pp. 51–56.

[12] Foster, Proceedings of Society for Advancement Clinical Investigation, 1910, p. 4 to 6.

complicated and in many of its aspects by no means clear. In the first place, amino-acids resulting from the protein digestion are possibly not absorbed entirely as amino-acids, but are reconstructed into more complex bodies allied to proteins (peptids) before entering the blood stream. If this hypothesis is in any degree true it would have a bearing on results deduced from the administration of amino-acids by the mouth. When the latter bodies are perfused through the liver by means of the blood channels, however, they are broken down in several ways; arginin, for example, yields urea by simple cleavage, but is exceptional in this respect. Other acids, such as leucin and glycocoll, are primarily deamidized with the formation of urea from the amino radicle as a by-product. The formation of urea itself from these radicles is a step that is not clearly explained.[13] In view of these experimental facts the excretion of amino-acids in the urine in the severest types of liver degenerations, yellow atrophy and phosphorus poisoning, are in a degree comprehensible, and in such conditions it matters not whether the products excreted are unchanged substances derived from digestion or are primarily autolytic. But where the liver cells are not so gravely injured as in the above states the urinary findings may be quite different. Jackson and Pearce[14] found an increase excretion of ammonia with corresponding fall in urea in dogs with diffuse hepatic degeneration induced with hemotoxic sera. The absence of a marked rise in the rest nitrogen (amino-acid-N) in these experiments suggests that the liver had retained its deamidizing function while that of urea formation was impaired. It is evident from these observations with two forms of liver derangement that no deduction can be drawn *a priori* as to what function will be found predominently deficient in human cirrhosis. Glaessner[15] presumed that in cirrhosis there would be a loss in some degree of the deamidizing power of the liver and fed to patients with liver diseases amino-acids. By a method of separation which Glaessner devised he believes he has recovered from 20 to 70 per cent. of the ingested acids in the urines of cirrhotic cases, while normally none is recovered, as it is all converted to urea and excreted as such.

In my duplication of Glaessner's tests his method of recovery was not employed because it did not seem in any way reliable; the rest nitrogen in the urine offering more trustworthy results. Three severe cases of atrophic cirrhosis were studied. They were given an exclusive milk diet in definite daily amounts and all of the urine collected in twelve hour specimens. Aspartic acid was given to two individuals and alanin to one. These substances were administered in 15 gram doses before breakfast. The nitrogen partition of the urine following this experiment in none of the cases deviated from the normal sufficiently to warrant the deduction of unchanged

[13] Hahn, Massen, Nencki, and Pawlow, Arch. f. exp. Path. und Pharm., 1893, xxxii, p. 161.
[14] Jour. Exp. Med., 1907, ix, 567.
[15] Wien. med. Woch., 1907, lvii, p. 1034.

excretion of the amino-acid fed. These results were not encouraging, and since an autopsy on one of these cases disclosed as extreme a grade of cirrhosis as one is likely to encounter, this line of investigation was abandoned.

Recently an interesting communication has appeared from Falk and Saxl[16] dealing with amino-acid secretion in cirrhosis. These authors fed alanin and glycocoll, usually the latter, and believed they recovered large percentages of the ingested substance in the urine in cases of cirrhosis. The criticism of their results rests upon their method of estimating amino-acids in urine. The method employed, that of Sörensin,[17] is by no means accurate, and under some conditions the error is enormous. The choice of glycocoll (the one most used) as an amino-acid, the recovery of which was to be estimated by this method, was particularly unfortunate, since it has been pointed out that with this substance error is most liable, and most difficult to prevent.

The only way at present of determining the amino-acids in urine with any pretence of accuracy is by means of a complete nitrogen partition—the "rest" nitrogen then contains the amino-acid nitrogen. It is also necessary that the diet be the same throughout the period of observation, as this is a factor in the amount of "rest" nitrogen. With a few exceptions, the tables of Falk and Saxl are not very convincing as they stand.

While working with dogs with Eck fistulas,[18] certain peculiarities in the creatin and creatinine metabolism were noticed, which suggested that perhaps these substances were sufficiently dependent on the liver for their formation to make them serve as indicators of hepatic sufficiency. It will be recalled that Mallenby[19] regarded the excretion of creatin as significant of liver disease, but his cases were mostly neoplasms, wherein rapid tissue loss is a complicating factor. In my series of cases the only divergence from normal, either in finding creatin in the urine with milk diet or in the recovery of creatin or creatinine fed to patients, was when the patients had arrived at a cachectic stage in the disease. When there is a relatively rapid loss of tissue creatin appears as a urinary constituent, but this fact is not peculiar to liver disease, as it occurs in fevers also.

The fundamental question involved in securing a function test for any organ depends primarily on the discovery of some activity which is peculiar solely to the organ involved. In the case of the liver its more obvious functions, as the secretion of bile, are performed even when disease has made considerable progress, which fact is in entire accord with the number of apparently healthy cells found in cirrhotic livers at autopsy. The finer activities of

[16] Zeit. f. klin. Med., 1911, lxxiii, p. 138.

[17] Henrique and Sörensin, Zeit. f. physiol. Chem., 1909, lxiii, p. 29; Malfatti, ibid., 1910, lxvi, p. 163.

[18] Foster and Fisher, Jour. Biol. Chem., 1911, ix, 559. [19] Jour. of Physiol., 1908, xli, 447.

these cells, which, presumably, would be the first to suffer in diseased states, are, so far as known at present, either in part assumed by other tissues, or else the cells can endure some injury and still remain physiologically efficient. Endeavors then to elaborate tests along the lines of those discussed in this paper are hardly likely to meet with success, and particularly is this so, since what is required in clinical medicine is not only a means of confirming the diagnosis of an evident malady but especially of detecting a morbid process in its earlier stage.

THE MANAGEMENT OF ASTHMA IN CHILDREN.

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The proper care of these cases naturally implies a knowledge of the causes, nature, and clinical varieties of asthma. The diagnosis is certainly more difficult in infants than in adults, as there is no standard whereby there can be any uniformity of opinion as to what is meant by asthma in infants. Undoubtedly many cases go astray under other names, as capillary bronchitis. The writer has often been surprised in thinking he had an acute congestive pneumonia, to find on the following day all symptoms had subsided. After two or three experiences of this kind, in the same child, one will realize he is not dealing with an inflammatory process.

Asthma is a symptom rather than a disease, and has no real pathology in the sense that there is no characteristic lesion constantly present. For this reason it is difficult to give a correct definition. Most succinct is the one given by Holt, namely: Asthma is a vasomotor neurosis of the respiratory tract. All writers agree that neurosis is the important predisposing factor, and in adults it is often the sole cause of an attack. However, in infants and children there is usually some congestion of vasomotor origin or an acute inflammation of the respiratory tract. In 20 cases of which the writer has notes, that have been under his care during the last twenty years, there was but one in which the paroxysms developed without some preceding evidence of catarrhal inflammation.

Three elements probably enter into the immediate cause of the paroxysm.

1. Spasm of the bronchioles; the muscular coat of the small bronchi consists of interwoven layers of longitudinal and circular fibers. The latter are the stronger, and under the influence of stimuli are capable of contraction with consequent lessening of the lumen. Brodie and Dixon have proved that stimulation of the

vagus by pilocarpin or electricity cause symptoms analogous to asthma.

2. Swelling of the mucous membrane lining the smaller tubes, either as an irregular turgescence or an edema, like unto that of urticaria. Further evidence of this is found in the fact that with relief of the paroxysm there is an increased secretion of viscid mucus. This mucus often contains cellular crystalline elements, although the so-called Charcot crystals are less frequent in infants than in adults.

3. The loss of resiliency of the pulmonary air vesicles whereby the residual air increases in volume, with the consequent lessening in the volume of tidal air, producing the partial stasis of air in the lungs. A striking evidence of this is the markedly distended chest, observed in certain cases. It seems to the writer most probable that this is the condition in those cases where there is a marked degree of cyanosis during an attack, and in whom there is evidence of emphysema during the intervals. It is certainly reasonable to believe that these causative elements vary in different cases, or in the same case in different paroxysms. If not, on what hypothesis are we to explain why one case is relieved by morphine, another by adrenalin, and yet another by oxygen?

When we come to study the symptoms it will be found there are three common to all cases, and when these three symptoms are associated they certainly indicate asthma.

1. The periodicity of the attacks, that is, similar attacks recurring in the same patient.

2. The dyspnea, which is expiratory in character, is in marked contrast to inspiratory dyspnea of spasmodic or diphtheric croup.

3. The wheezing breath sounds heard on auscultation and frequently audible at some distance from the patient.

Other symptoms observed in certain cases are distention of the chest, giving a full rounded appearance, the so-called barrel shape. The diaphragm is usually depressed and often fixed or immovable. It will generally be noted that the child is unwilling to talk. Even in infants the countenance has an anxious appearance, and during the severity of the paroxysm the skin is covered by a cold perspiration. The muscular effort in breathing is manifest by the play of the auxiliary muscles.

Upon auscultation there is heard a wheezing stridor, less audible at a distance from the body in infants than in children. Sonorous and sibilant rales are heard over all parts of the chest. The percussion note is usually hyperresonant. The respirations are sometimes below normal in frequency, and often the pause at the end of inspiration is shortened. In infants suffering from asthma, however, the respirations are often rapid as in bronchopneumonia. Indeed, in infants the diagnosis will often hinge upon the sudden relief of the symptoms, and tendency to recurrent attacks. A

valuable aid to the diagnosis of asthma in infants, that should be more frequently employed is the blood count. Holt in his textbook makes the following statement: "The blood picture in asthma is characteristic and has much value in the diagnosis. The important thing is the presence of a large number of eosinophile cells. They may form as high as 15 to 20 per cent. of the leukocytes. In a series of cases examined in my clinic by Wile the average was 10.7 per cent. The highest was 26 per cent. The eosinophilia is greatest at the height of the attack. The blood examination serves to differentiate asthma from simple bronchitis and tuberculosis. The existence of the eosinophilia definitely shapes the asthmatic character of these attacks in frequency."

As the management of the individual case will be influenced by the cause, a few words concerning the etiology will aid in the treatment. There is certainly an hereditary tendency. Of the 20 cases that have been under the author's care during the last twenty years, in the greater number there was a history of asthma, either in the ancestors or in the collateral line. In some cases there was a history of some nervous affection, as migraine or epilepsy, and in some cases both a neurotic and asthmatic history, and in others a distinct history of rheumatism in one or other parent. Kerley, in his book on the *Treatment of Children*, attaches much importance to the rheumatic history, and in the treatment of these cases, strongly recommends specific antirheumatic treatment.

Season has a decided predisposing influence. In the writer's experience the attacks are most frequent in the winter and spring. This applies to infants and children more than to adults, for in the latter, attacks are said to be more frequent between fall and spring. The probable reason for this is that attacks in children are usually excited by acute coryzas or bronchitis, and children are more susceptible to these catarrhal conditions during the colder and more changeable months of the year.

There are undoubtedly many exciting or reflex causes that are sufficient to induce the paroxysm, and careful search for the irritation that leads to the attack should be made in each case. There is undoubtedly some relation between asthma and eczema or other skin lesions. The writer has one child under observation who never has asthma when the eczema is active. Diphtheria antitoxin has been known to produce asthmatic paroxysms and the writer has had one personal experience of this kind in the use of antitoxin. In this case an immunizing dose of 500 units induced the paroxysm. In some cases, the paroxysms are undoubtedly caused by acute indigestion, probably due to the absorption of some toxin from the intestinal tract. Fisher, of New York, attaches much importance to this as a cause, and suggests the theory that the pressure against the stomach and diaphragm is sufficient to

excite an attack. The influence of adenoids, hypertrophied tonsils, thickened turbinates, and spurs on the septum should receive careful attention. Experience has shown that there are certain sensitive points in the mucous membrane of the nose that reflexly induce asthmatic attacks. However, it does not follow that the removal of these conditions will prevent future attacks. It is a safe rule to follow that if these conditions would demand surgical treatment in other children, they should be treated in asthmatic children. The influence of enlarged bronchial glands in causing asthma in children is difficult to determine, but it is entirely reasonable to believe that these glands may induce such attacks. Indeed, any abnormal condition in any part of the body that might in any way act as an irritant, should receive careful consideration. Children are less likely to have attacks induced by irritation of the nerve filaments in the respiratory tract, by odors from animals or plants, than adults. Also, they are less likely to be influenced by psychical impressions.

The management of asthmatic children naturally resolves itself into two divisions, namely, the care and treatment of the child during the intervals, and the treatment during the paroxysm. The asthmatic child is entitled to fair play. Each case, therefore, should receive a thorough examination, including an inspection of the entire body, noting any physical defect, with careful examination of the nose and throat. A thorough investigation should be made of the nervous and digestive systems including the diet, mode of eating, and, indeed, a physical examination of all the vital organs. An examination of the urine and a blood count should be made in each case. The history of the child and family should always be obtained. In this way valuable hints as to treatment are usually ascertained. It should be borne in mind that the treatment is directed to the patient rather than to the disease. For example, in one of my patients the only abnormal symptom gathered from a careful examination was the presence of indican in the urine. Having gathered all the facts obtainable, a careful outline of treatment, including diet, habits of the child, etc., should be specifically given to the mother. As to clothing: I would simply urge two points, namely, that the feet and legs should always be kept warm and dry, and the chest and neck properly protected to prevent catching cold. In most cases, I have found specific directions as to the diet necessary to the progress of the case. Generally a low meat diet with a high vegetable proteid. In cases induced by intestinal trouble, the diet should contain green vegetables and fruit juices. As has already been indicated, in the majority of cases the paroxysm has been induced by an acute attack of bronchitis. Hence, it is important in all cases that the mother should take prompt measures for relief upon the first symptom of a cold, as sneezing or coughing. My rule is that the child is to be

put promptly to bed, have the diet restricted to liquid foods, and given an active cathartic to move the bowels freely. Medication will naturally vary in individual cases, but hot drinks are always indicated. I have one patient in whom a dose of quinine certainly aids in aborting a cold, and another patient in whom a dose of quinine will induce a paroxysm. This has been proved several times.

There are certain cases that fail to respond to our best efforts, and in these cases a change of climate is necessary. This is often a serious problem because a change of climate may mean a change of location for the parents. From my experience in 2 cases, a change of climate for one winter was sufficient, and these cases returned to their homes and have passed several winters without recurring attacks. The writer has known of cases where a change in location of only a few miles has been sufficient to prevent the attacks. It is impossible to explain, on rational grounds, why this is true. If there is simple anemia, suitable treatment should be instituted. In cases where there is a history of rheumatism, either in the child or parents, appropriate treatment should be adopted. An instructive case of this kind will be found in Kerley's work on the *Treatment of Children*. The writer has had one case showing the benefit derived from this line of treatment. Two years have now passed without an asthmatic attack. The writer firmly believes in a system of pulmonary gymnastics for asthmatic children. The mother is instructed to give the child daily exercises in deep breathing. These exercises are to be given at regular hours, with special emphasis laid upon the importance of complete expiration. This is particularly valuable in those children in whom there is a vesicular emphysema as a result of the asthma. These children should avoid running up hill, and all violent exercises. In these cases, I wish to strongly recommend an elastic binder, worn around the chest and held in place by means of shoulder straps. This should be tight enough to exert a constant slight pressure. Its value resides in the fact that the pressure aids in expiration. Any intelligent mother can easily make this binder. The writer has personal experience with its use in 2 cases.

In many cases there is a catarrhal bronchitis, persisting after the cessation of the acute paroxysms, often with wheezing on slight exertion, and it is important to clear up this condition. In these cases the writer has found decided benefit from the use of sodium iodide. The remedy should be continued for several weeks. It should be given in doses of from 2 to 4 gr., three times daily, after meals, in essence of pepsin. There are other cases with cough, but without the nervous element, who are greatly benefited by the syrup of hydroiodic acid. The U. S. P. formula may be given in doses of from 10 to 20 minims. This is of special value where there is a general adenopathy or evidence of enlarged bronchia

glands. This remedy I have given in several cases and am convinced of its value. It is more acceptable to the stomach than other preparations containing iodine.

TREATMENT OF THE PAROXYSM. "The utter capriciousness of asthma in its response to the action of drugs, renders our course largely empirical, so that in many cases, in hope of finding one that will succeed at last, one drug after another is tried only to be discarded as useless."[1] While it is to be hoped that the modern study of anaphylaxis will shed light on prevention and treatment of asthmatic attacks, for the present, at least, the physician must be guided by clinical experience. While there is little danger to life in an acute attack, yet there is real suffering to the patient and anxiety to the parents, who naturally look to the physician for relief. In my experience the fumes from the various asthma powders do not give relief to infants, but on the contrary often aggravate the symptoms by increasing the cough. The room should be warm. Air currents are to be avoided. The condition may be made worse by changing from a warm to a cool room. At the same time fresh air is necessary. Ventilation may be had from an adjoining room rather than from open windows in the room. Only necessary attendants should be allowed in the room. If the bowels are distended with gas they should be relieved promptly by a warm enema. If the paroxysm occurs soon after a hearty meal, then a prompt emetic will afford relief.

In the writer's opinion the following cases illustrate the value of different remedies, and seem to prove that one drug will not relieve all cases. In 2 cases, the writer has given adrenalin solution hypodermically. In both cases the relief was so prompt as to leave no doubt as to the value of the remedy. On the other hand, the writer has seen it utterly fail. The dose for infants is from 3 to 5 minims of the $\frac{1}{1000}$ solution of adrenalin chloride.

The writer has attended one little patient a number of times, without any remedy giving relief, until morphine sulphate, $\frac{1}{30}$ grain, was tried. Then in subsequent paroxysms this drug gave relief each time it was given. In another case chloral hydrate gave prompt relief. Other remedies had been given by me in previous attacks. In that case, 3 grains were given and the dose repeated in an hour. After the second dose this child was enabled to lie down and breathe with comfort. In one of the most severe cases the writer has ever seen the inhalation of nascent oxygen gave quick relief. This child was cyanotic, with cold, clammy skin, and short, panting breathing. The attacks came on without any preceding evidence of bronchitis. The oxygen was administered during three separate paroxysms, and always with prompt relief. In this particular case the attacks ceased at the age of five years and only recurred in a

[1] Osler's System, iii, 720.

lighter form at the age of eighteen years. At the time this patient was under my care a local druggist had an apparatus for the extemporaneous preparation of oxygen, so that it was possible to apply the remedy promptly.

In Osler's *System* the use of atropin hypodermically is recommended in doses sufficiently large to produce the physiological effect, but the writer has had personal experience with the remedy in only one case. The skin became flushed, but without marked relief.

There are cases in which after the severity of the paroxysm is relieved there remains a cough, with more or less wheezing and short breathing on exertion, that requires further attention. Here the use of heroin in a syrup of hypophosphites will often benefit by relieving the cough. In some cases in which the cough disturbs sleep, a single dose of antipyrin given at bedtime, will allay the cough and induce quiet sleep. The writer distinctly recalls 3 cases in which this remedy acted well after there had been no benefit from other drugs.

It is difficult to estimate the value of inhalations, but where there is a dry, teasing cough this treatment should be employed. The value of the treatment resides in the fact that the inhalation of moisture promotes expectoration. The use of a croup kettle is necessary, as it is neither possible nor best to saturate the room with steam. A number of remedies may be used in the steam. The writer prefers a combination of creosote and oil of eucalyptus, one teaspoonful of the mixture in a pint of water. The use of this combination with an improvised croup tent, for one-half hour at a time, and repeated two or three times in twenty-four hours, will often soften the cough and induce expectoration. Inhalations of lime water also will be of benefit.

Following the paroxysm of asthma, and until the cough is relieved, these children should receive very careful general care, including a restricted diet, attention to elimination, and careful regulation of the temperature and ventilation of the room, and proper covering to the body on going outdoors.

Conclusion. Basing my experience upon the study of the 20 cases mentioned in this paper, it is correct to affirm that the majority of infants and children suffering from asthma, ultimately recover. The writer has recently received reports from 10 cases that had been under his care in past years. In 8 cases there had been no return of asthma, and in the other 2 the paroxysms were lighter than in former years. The frequency and severity of the paroxysms can in a large measure be controlled by proper care and treatment. A limited number develop an emphysema, and as a result their general growth is permanently impaired. This is the most serious sequel of asthma, and because of this, all cases should receive prompt treatment, with a view of lessening

the severity and frequency of the paroxysms. The general care of asthmatic children is important, because in most cases a careful study will reveal some exciting cause that can be removed, or some morbid condition, as constipation or indicanuria, that can be corrected. Attention to these suggestions with diligence in discovering and removing other possible causes, will enable many asthmatic children to enjoy comparative freedom from attacks, and to develop into happy, useful citizens.

THE TREATMENT OF FRACTURES OF THE FOREARM, WITH NOTES OF THE END RESULTS OF 52 CASES TREATED WITHOUT OPERATION.[1]

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Nearly four years ago, in a paper discussing the end results of 61 cases of fracture of the femur, treated without operation, which was presented before this Academy,[2] it was stated that it seemed incumbent on those surgeons who advocated operative treatment as a matter of routine in cases of recent fracture "either to demonstrate the evil results which they regard as a necessary consequence of accepted" (that is, non-operative) "methods, or to bring forward proof that by operation still better results can be obtained, and without unjustifiable risk to the patient." It was further stated: "The advocates of operative treatment, in short, should either be able to show that the methods they propose will not increase the immediate mortality and will greatly diminish or altogether prevent the unfavorable results of conservative treatment; or, failing this, they should at least convince conservative surgeons that the functional results of the accepted forms of treatment are such as can no longer be tolerated."

To our knowledge no series of cases has been published, of fractures of any long bone in the body, demonstrating either the inadequacy of conservative measures or the superiority and equal safety of operative treatment. It is to show that a fairly large series of cases of fracture of the forearm, involving both bones

[1] Read before the Philadelphia Academy of Surgery, February 5, 1912.
[2] Ashhurst and Newell, Annals of Surgery, 1908, ii, 748.

in some part of their shafts, may be treated with satisfactory results without a single resort to operation, that we now present a study of these 52 cases. From this series are excluded cases of fractures involving the elbow or the wrist joint, and cases of Colles's fracture of the radius complicated by fracture of the ulnar styloid. Fractures of the forearm, thus limited to injuries of the shafts of the ulna and radius, do not form a large proportion of the cases of fracture seen, but they have been selected for this analysis because, next to those of the femur or leg bones, they are at present the type most often (and we believe usually quite unnecessarily) subjected to operation.

These patients were treated in the services of one of the writers at the Episcopal Hospital and at the Children's Hospital. In almost every case the patients first apply for treatment out of dispensary hours, soon after the accident which produced the fracture. They are dressed then by the surgical interne on duty in the receiving ward at the time, skiagraphs are made, and the patients are referred to the out-patient department for further treatment. Although in the very busy dispensary services in which they are treated it is not always practicable, our aim always has been to examine and dress with our own hands *all the recent fractures*, and to continue to dress them with our own hands *until union is fairly firm*. We have never relegated any cases of fracture to the care of orderlies or nurses, nor have we ever turned them over to the internes until we have ascertained by repeated and persistent personal instruction and supervision that the particular interne on duty was capable of applying the dressings in a satisfactory manner. In the treatment of fractures, as in many other important departments of surgery, one must remember that "eternal vigilance is the price of safety."

REDUCTION. "Reducing" a fracture is a relative term, since comparatively few broken bones can be accurately restored to their original form; and in the case of *shafts of long bones* it is not always necessary that reduction should be accurate. Nevertheless, the aim must be to secure as accurate reduction as possible, and in the case of fractures near joints (especially the elbow) accurate reduction is extremely important; but in the middle of the shaft of a long bone it is sufficient to secure *firm bony union*, with *no appreciable shortening*, and with *preservation of the normal axis of the limb*. For the first and second results to be obtained it is necessary for the fragments to be in contact "end-on," not only by lateral contact; and for the lateral displacement, not to exceed two-thirds of the diameter of the bone.

Anesthesia rarely will be necessary in reducing a fracture of the forearm if the surgeon takes advantage of the relaxation of the muscles which may be secured by position of the limb. *Full supination of the forearm* is the position preferred, with the elbow

flexed to a right angle. Correct replacement of the ulnar fracture usually can be determined clinically, as this bone is subcutaneous; but the radius is buried among so many muscles that a skiagraph frequently is necessary to ascertain the position of the fragments if the fracture is above the middle of the bone.

The forearm is then dressed *in full supination*[3] between two straight splints, specially cut to fit each individual patient. They should be a little wider than the forearm, so as to prevent crowding the bones together laterally, but not so wide as to permit rotation of the forearm within the splints. The palmar splint extends from the bend of the elbow to the tips of the fingers, while the dorsal splint extends from the olecranon to the wrist. These splints should be smoothly but thickly padded with raw cotton. A longitudinal pad placed between the bones, in an effort to wedge them apart is not only useless but harmful. Extra compresses, however, may well be placed over any of the fragments that tend to project. The splints are then strapped snugly around the forearm by bands of adhesive plaster at the wrist and below the elbow, and are held securely in place by a roller bandage. A large "handkerchief" or "triangular" sling is applied, supporting the forearm throughout its length, and the forearm is carried against the chest, but always in full supination. In very small children, and in adults where the seat of fracture is near the elbow, this joint is immobilized by employing an anterior angular splint, known in Philadelphia as Hartshorne's, instead of the straight palmar splint.

The position of full supination is employed not only because supination is the most difficult part of rotation to regain,[4] if once lost, and because the upper fragment of the radius usually is kept in supination by the biceps; but because it was found by one of the writers when the forearm was dressed in mid-pronation, as commonly advised now, and as formerly employed by him, that the fragments sagged by the force of gravity, and that the patients recovered not only with lost supination, but with angular deformity of both bones toward the ulnar side. If attempt is made to correct this deformity by adjusting a coaptation splint over the angular projection of the ulna, this may indeed be overcome, but the surgeon will succeed merely in forcing the ulna nearer the radius which cannot be influenced by such an appliance; and the dis-

[3] According to Malgaigne (Fractures, Paris, 1847, p. 591) this position was condemned by Hippocrates, though used by his contemporaries. Its advantages were pointed out by Paré, who was opposed to the semi-prone position until he learned that the latter had been approved by Hippocrates, whereupon Paré resumed the use of the semiprone position. Malgaigne thought he was himself the first of modern surgeons to return to the use of full supination, advised in his Anatomie Chirurgicale (1838), until he learned that Lonsdale (London Med. Gaz., 1832, ix, 910) had preceded him.

[4] The patient regains pronation by active use of the hand; very few motions require extreme supination.

ability as regards rotation will be increased. However, fractures in which no tendency to displacement exists, such as greenstick and subperiosteal fractures, may be treated successfully in the semi-prone position.

Often it is exceedingly difficult to keep these fractures even approximately reduced during the first week or ten days; and it is during this period that impatient surgeons are apt to urge operation as the only solution of the difficulty. But usually a little better position can be secured at each dressing, and when the ends of the bones begin to become sticky, during the second week, it will be found that deformity daily becomes less, and what looked at first (to the inexperienced) like a hopeless case, will result in a very useful arm, and one with slight or with no visible deformity. Skiagraphs are valuable and interesting, but a surgeon never should be terrified by the appearance of the forearm bones in a skiagraph into thinking that only operative treatment can give his patient a good result. If he uses the eyes in the ends of his fingers, he will secure by conservative means quite as good, and in many cases a much better result than by operation, and in a shorter time.

AFTER CARE. This involves removal of the dressing frequently enough to make sure that the soft parts are in good condition, and that reduction is maintained by the dressings employed. The surgeon never should neglect to see the patient on the day after the dressing is first applied, and to ascertain for himself that the limb is in good condition, and that the dressing is comfortable. An uncomfortable dressing always is inefficient, even if not positively harmful; but if the dressing is comfortable it is not desirable to redress the limb more than two or three times weekly at first, and less often as union progresses. As the splints and bandages are being removed for re-dressing, the patient sits facing the surgeon, and the forearm lies supine on the patient's thigh. The palmar splint is lifted carefully off without moving the forearm, and the flexor surface and sides of the forearm and hand are gently bathed in dilute alcohol; then without rotating the forearm at all it is gently raised as a whole from the dorsal splint, and the extensor surface is bathed similarly, correct apposition of the fragments being maintained all the time. Any undue haste or rapid movement or attempts at rotation will be painful, will evoke muscular spasm, and may cause displacement of the fragments.

We do not approve massage or mobilization in the treatment of fractures, except in so far as they are unavoidable in procuring proper care of the soft parts; and while we acknowledge the truth of the dictum of Lucas-Championnière that "a certain amount of motion between the fragments encourages the formation of callus," we are firmly of the opinion that even the most careful immobilization by splints allows, and proper care of the soft parts,

as above indicated, provides that "certain amount" of motion which is desirable; and that any surgeon who attempts more, in the vain idea that he is following modern teaching, will succeed either in stirring up such an amount of callus (especially in children) as to cause deformity and injurious pressure on the soft parts, or (in most adults) will leave his patient with an ununited fracture.

When the ends of the bones become "sticky" and no tendency to displacement exists, the surgeon may then begin to make very limited degrees of passive motion in the neighboring joints at each dressing, meanwhile maintaining support at the seat of fracture. Under no circumstances should the passive motion cause pain. When union is firm enough for all external support to be discontinued, function usually will be more comfortably and quickly recovered by active movements by the patient himself, than by further attempts at psssive motion; and if a fracture has been treated properly in the first place, massage very rarely will be necessary to accelerate the cure.

Operative Treatment of Simple Fractures. We believe there are only two indications for the "open method" of treating simple fractures: (1) If the fracture cannot be properly reduced without operation, and (2) if proper reduction cannot be maintained without direct fixation of the fragments.

1. *When Proper Reduction is Impossible.* Impossibility is here a relative term, since what is impossible for one surgeon may not be so for another; and the qualification "proper" reduction is employed because we do not wish to imply that operation is indicated whenever accurate, exact, perfect, anatomical replacement is impossible, but only when such degree of reduction, as has been described in a previous paragraph as requisite for proper function, cannot be secured without open operation. Less perfect reduction is requisite in children than in adults, since in the former compensation is more rapidly established; and oblique fractures require less close and accurate apposition of their ends than do transverse fractures.

2. *When Subsequent Displacement Cannot be Prevented.* This also is a relative condition, depending on the skill of the surgeon in devising and applying efficient retentive apparatus, and upon the extent to which displacement occurs.

After operation the process of union often is slower than it would have been if no operation had been employed; and in a fair proportion of cases operated on by the average surgeon a mild degree of infection occurs, and only fibrous union results.

Statistics. These cases form a continuous series, absolutely unselected, running through a period of ten years. Of 66 patients treated, the end results are known in 52 cases; 43 of the fractures occurred in males, and only 9 in females. None of the female patients was older than fifteen years. Of the males, 31 were less

than fifteen years of age, and 12 were older. The youngest patient (a girl) was seventeen months old, and the oldest (a man) was fifty-seven years. The right and left arms were affected nearly with equal frequency.

For estimating the power of rotation, a special instrument (Fig. 1) was devised, and was constructed for us by D. W. Kolbe Co. For establishing a standard, the average normal rotation was ascertained by testing one hundred normal forearms of fifty persons (25 male, 25 female). The instrument consists of an indicator, kept vertical by gravity, and centred on a circular protractor. This protractor is attached to an upright board which itself is

FIG. 1.—Pronometer, or instrument for measuring the degree of pronation and supination. Indicator points to zero degrees in supine position.

fastened at right angles to a horizontal board. The horizontal board is strapped on the flexor surface of the wrist, the forearm being in full supination. In this position the indicator points to 0 degrees. If still further supination is possible, this is recorded as a *minus* quantity, of say 5, 10, or 15 degrees. As the forearm is rotated into pronation the protractor also rotates, but the indicator remains vertical and passes over the rotating scale from 0 degree up to 135 degrees or 140 degrees or more, according to the extent of pronation possible (Fig. 2). During this examination, it is needless to say, the patient's humerus should be kept immovably applied to the side of the thorax, and no deviation of the body from the vertical should be permitted.

NORMAL ROTATION. Our examination of 100 normal forearms gave the following results:

Ages varied from fourteen to seventy-seven years; average age, twenty-nine years.

Supination: Greatest . . . —45.00 degrees. Least . . . . 15.00 degrees.
Average . . . —11.72 degrees. { In males . . . — 7.42 degrees. In females. . . —16.02 degrees.
Average of right forearm —7.24 degrees; of left —16.2 degrees.

Pronation: Greatest . . . . 180.00 degrees. Least . . . . 120.00 degrees.
Average . . . . 147.77 degrees. { In males . . . 148.24 degrees. In females . . . 147.30 degrees.
Average of right forearm, 147.24 degrees; of left, 148.00 degrees.

Greatest range of rotation in any one patient, from —45 degrees to 155 degrees, or 200 degrees.
Least range of rotation in any one patient from 0 degree to 122 degrees, or 122 degrees.
Average rotation from —11.72 degrees to 147.77 degrees, or 159.49 degrees.

FIG. 2.—Pronometer. Indicator points to 90 degrees when forearm is in "mid-pronation."

RESULTS. In studying the end results of these 52 cases, it may first be stated what was not secured: there was no case of gangrene of the soft parts or of necrosis of the bones; there was no case of ischemic contracture; none of nerve lesion; none of ununited fracture; none of conspicuous deformity. There was one case of delayed union (Case 37), but this patient cured himself, by returning to his work as a blacksmith at the end of ten weeks. There were several cases in which some thickening or irregularity could be felt at the site of fracture; but none in which these were appreciable at a glance. There was no case of disability, even slight. And these results were obtained without excluding 9 more or less complicated cases, as follows: 1 case of badly comminuted fracture (Case 39); 1 case of fracture of both bones of both forearms (Cases 2 and 3); 3 cases of multiple fractures of the upper extremity (Cases 1, 25, 26) involving both the humerus and the bones of

the forearm, two of which were compound comminuted fractures; as well as 3 other cases of compound fracture (Cases 7, 32, 47). None of the cases of compound fracture, however, was such as to require operation on account of the condition of the soft parts.

The end results may be seen at a glance in the following table. Under the heading "perfect result" we include only such cases as have recovered without palpable deformity, and with preservation of perfect function. If, in spite of preservation of perfect function, there is palpable deformity, as in Cases 2 and 3, the patients are recorded in the second column, as "slight deformity, but perfect function." If there is limitation of function the cases are placed in the third column; in none was there any limitation of function except in rotation; and in none was there any disability.

END RESULTS OF FIFTY-TWO CASES OF FRACTURE OF BOTH BONES OF THE FOREARM.

Character of fracture.	Class I. Perfect result.	Class II. Slight deformity.	Class III. Rotation limited.
Greenstick	10	1	0
Simple complete	22	8	4
Simple comminuted	0	0	1
Compound	1	1	1
Compound comminuted	1	0	2
Total	34 (65.4%)	10 (19.2%	8 (15.4%)

The skiagraphs of end results, which we have chosen for reproduction here, are those of cases in which the prognosis seemed least favorable, and represent, therefore, much worse than the average skiagraphic results. As far as cosmetic results are concerned, there was no visible deformity in any of these cases except in Cases 2, 3, 26, 39, 48, and 51; and in these patients a mere glance at the bared arm will not detect any deformity.

In Class 1 we have included Cases 1, 4, 5, 6, 8, 10, 11, 12, 14, 16, 17, 18, 19, 22, 23, 24, 25, 27, 28, 29, 31, 34, 35, 36, 37, 38, 41, 42, 43, 44, 45, 46, 50, 52.

In Class II are included Cases 2, 3, 20, 21, 30, 33, 40, 47, 48, 49.

In Class III are included Cases 7, 9, 13, 15, 26, 32, 39, 51.

We are greatly indebted to Dr. Thos. S. Stewart, radiographer to the Episcopal Hospital, and to his assistant, Dr. A. R. W. Wilkinson, for the interest they have taken in providing us with numerous skiagraphs for the purpose of this study.

ABSTRACTS OF CASE HISTORIES.

CASE 1.—Michael C., aged fifteen years. May 6, 1902. Episcopal Hospital. Multiple fractures of right upper extremity (surgical neck of humerus, both bones of forearm, compound of ulna). Recorded as Case I in a paper on "Multiple Fractures" (Ashhurst,

Annals of Surgery, 1907, ii, 263). Full supination. Examined February 20, 1907. No visible or palpable deformity anywhere. Does heavy laboring work, and would not know arm ever had been injured. Perfect result. Class I. (Fig. 3.)

FIG. 3.—Case I. Five years after compound fracture of both bones of forearm, and fracture of humerus. No deformity. Perfect function.

CASES 2 and 3.—Augustus F., aged thirty-five years. March 16, 1903. Episcopal Hospital. Fracture of both bones of both forearms, sixteen days previously; has been dressed on internal angular and short dorsal splints, in position of mid-pronation. Arms gave constant pain. No attempt at union, because fragments were not in contact and were not immobilized. By putting forearms in full supination better position was secured, but complete reduction was impossible. However, pain was immediately and absolutely relieved. Two weeks later, good union. Examined October 28, 1911. Says he never knows arms were broken; was out of work only fourteen weeks in all, and has worked as machinist ever since with perfect function. There is no visible deformity, but the displaced fragments are still palpable. Supination in both forearms complete; pronation on right to 135 degrees, and on left to 130 degrees. Without seeing the skiagraphs made recently (Figs. 4 and 5), the results might be considered perfect. Class II.

CASE 4.—Harry H., aged ten years. September 1, 1903. Episcopal Hospital. Right. Treated in supination. Examined October 28, 1911. Full supination, pronation to 165. Class I.

CASE 5.—Phoebe G., aged two years. October 15, 1903. Episcopal Hospital. Right, greenstick. Examined October 28, 1911. Full supination, pronation to 160. Class I.

CASE 6.—Adolph W., aged ten years. October 19, 1903. Episcopal Hospital. Right. Examined, January 28, 1912. Broken

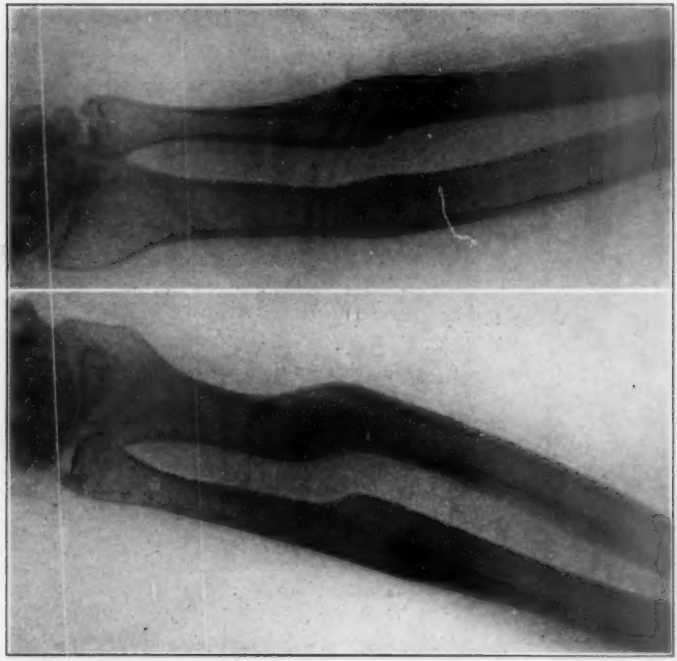

FIG. 4.—Cases II and III. Antero-posterior views of both forearms, eight years after injury. Function perfect.

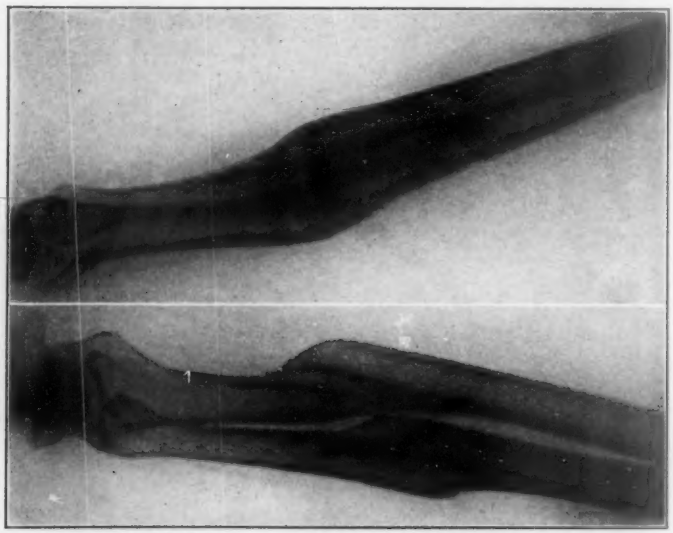

FIG. 5.—Cases II and III. Lateral view of both forearms eight years after injury. Function perfect. Patient first came under the writer's care sixteen days after injury.

arm, supination —20 degrees, pronation 130 degrees; normal arm, supination —15 degrees, pronation 135 degrees. Class I.

CASE 7.—William T. S., aged forty years. January 18, 1904. Episcopal Hospital. Right, simple of radius, compound comminuted of ulna. Examined five weeks later. Function good, but some limitation of supination. Class III.

CASE 8.—Fred. S., aged fifteen years. January 18, 1904. Episcopal Hospital. Dressed in full supination. Examined March, 1904. Class I.

CASE 9.—Thomas M., aged twenty-five years. January 19, 1904. Episcopal Hospital. Left, above middle. Great and persistent overlapping, with projection of upper fragments of radius and ulna on extensor surface. Dressed in mid-pronation, on internal angular and short dorsal splint. Examined March 12, 1904. Very slight deformity; no supination beyond mid-position. Class III.

CASE 10.—George H., aged twenty-eight years. January 23, 1904. Episcopal Hospital. Left, middle third. Dressed in mid-pronation. Examined, March 12, 1904. Class I.

CASE 11.—Emma L., aged two years. January 31, 1904. Episcopal Hospital. Greenstick. Examined March 3, 1904. Class I.

CASE 12.—William A., aged twelve years. April 12, 1904. Episcopal Hospital. Left, treated in mid-pronation. Examined October 28, 1911. Supination full, pronation to 135 degrees. Class I.

CASE 13.—Fred. H., aged sixteen years. April 15, 1904. Episcopal Hospital. Right, dressed in mid-pronation. Had refracture of same forearm in November, 1904. Examined January 27, 1912. No deformity, no disability. Right: supination, 25 degrees; pronation, 120 degrees. Left: supination, 20 degrees; pronation, 145 degrees. Class III.

CASE 14.—Albert S., aged thirteen years. September 1, 1904. Episcopal Hospital. Greenstick. Treated in mid-pronation. Examined October, 1904. Class I.

CASE 15.—James M., aged eight years. September 8, 1904. Episcopal Hospital. Left lower third. Very great cellulitis. Treated in mid-pronation. Examined October, 1904. No deformity, but little supination beyond mid-position. Class III.

CASE 16.—Thomas McG., aged fourteen years. December 7, 1905. Episcopal Hospital. Right; of radius above insertion of pronator teres, and greenstick of ulna, same level. Treated in full supination. Examined December 29, 1905. No deformity, full supination, pronation good. Class I.

CASE 17.—Anna D., aged fourteen years. December 23, 1905. Episcopal Hospital. Right. Treated in full supination. Examined January 15, 1906. Class I.

CASE 18.—John F., aged thirteen years. December 29, 1905. Episcopal Hospital. Middle third. Treated in full supination.

Examined October 28, 1911. Full supination, pronation 165 degrees. Class I.

Case 19.—Juliette J., aged eight years. July 3, 1906. Children's Hospital. Greenstick, middle third. Treated in full supination. Examined August 2, 1906. Class I.

Case 20.—Carrie C., aged six years. August 2, 1906. Children's Hospital. Injury two weeks ago at Atlantic City, and dressed in mid-pronation. On admission today, fracture at junction of middle and lower thirds of right forearm; no union, fair position; but bowing of ulna to extensor surface. Treated in full supination. August 21, union good, no deformity; full supination and pronation. Examined August 28, 1906. Upper fragment of ulna displaced slightly posteriorly; functions perfect. Class II.

Case 21.—John S., aged twelve years. August 6, 1906. Children's Hospital. Left, junction of middle and lower thirds. Fell from tree; was stunned. Upper fragment of ulna projects beneath skin of flexor surface; both lower fragments displaced toward extensor and radial surfaces. Treated in full supination. August 10. Deformity persists; pad over upper fragment of ulna. August 14. Position better; growing firmer. August 21. Position fair; bones firm. Examined September 5, 1906. Little deformity, no disability; supination and pronation complete. Class II.

Case 22.—William G., aged seven years. November 3, 1906. Episcopal Hospital. Left, greenstick, middle third. Dressed in full supination. Then patient visited another dispensary, and when splint applied there fell off of itself, he returned to Episcopal Hospital, November 19, with marked dorsal bowing of both bones. Bones were re-fractured, deformity reduced, and forearm dressed in full supination. Examined December 10, 1906. No visible deformity, but a little callus palpable over radius. Full supination and pronation. Class I.

Case 23.—Albert S., aged eleven years. November 15, 1906. Episcopal Hospital. Right, complete of radius, greenstick of ulna. Dressed in full supination. Examined December 12, 1906. Class I.

Case 24.—Hugh F., aged fourteen years. November 21, 1906. Episcopal Hospital. Left, above wrist. Full supination. Examined October 28, 1911. Supination complete, pronation to 180 degrees. Class I.

Case 25.—Andrew M., aged fourteen years. December 22, 1906. Episcopal Hospital. Left; compound comminuted fracture of both bones of left forearm with compound comminuted fracture of left humerus. (Reported as Case VI in paper on "Multiple Fractures," in *Annals of Surgery*, 1907, ii, 263.) Treated in ward for nine days, then in dispensary. Forearm dressed in full supination. Fig. 6 is from a photograph taken three months after the accident. Examined October 28, 1911. Supination and pronation

complete. No deformity. Figs. 7 and 8 are from skiagraphs made in January, 1912. Class I.

FIG. 6.—Case XXV. Compound comminuted fractures of both bones of left forearm, with compound comminuted fracture of left humerus. No deformity. Perfect function. See Figs. 7 and 8.

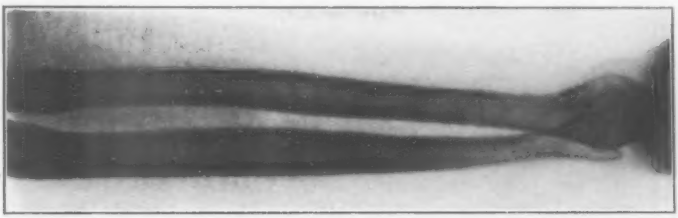

FIG. 7.—Case XXV. Lateral view of forearm five years after compound comminuted fracture of both bones.

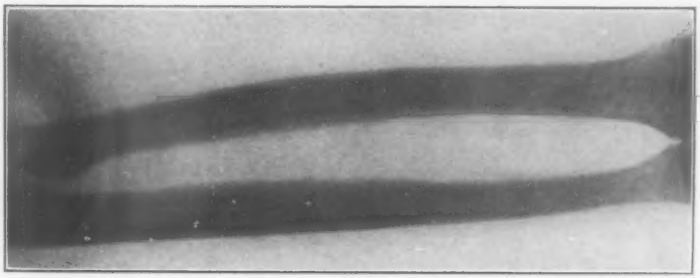

FIG. 8.—Case XXV. Antero-posterior view of forearm, five years after compound comminuted fracture of both bones.

CASE 26.—Henry D. E., aged fifty-seven years. November 26, 1906. Episcopal Hospital. Left. Compound comminuted fracture of both bones of left forearm, with comminuted fracture of left humerus. (Reported as Case V, in paper on "Multiple Fractures," in *Annals of Surgery*, 1907, ii, 263.) Treated with

forearm in full supination. Examined January 21, 1912. Was out of work (saw-maker) for four months. Complete function not regained for one year. Since then has experienced no disability whatever. There is considerable deformity in forearm, bones being bowed to radial side. Left forearm: supination, 0 degrees; pronation, to 85 degrees. Right forearm: supination, 0 degrees; pronation, to 155 degrees. Class III.

CASE 27.—Albert B., aged three years. March 5, 1907. Episcopal Hospital. Right, greenstick, two weeks old; bones bowed to extensor surface, some callus; inability to supinate completely. Refractured, and dressed in full supination. Examined April 4, 1907. No deformity, supination and pronation complete. Class I.

CASE 28.—Harriet B., aged two years. March 29, 1907. Episcopal Hospital. Left, greenstick. Full supination. Examined April 26, 1907. Supination and pronation complete. Class I.

CASE 29.—Charles G., aged fourteen years. January 9, 1908. Episcopal Hospital. Left, full supination. Examined February 13, 1908. Class I.

CASE 30.—Harry W., aged thirty months. July 8, 1907. Children's Hospital. Left, greenstick. One month's duration. Very marked angulation just above wrist, about 135 degrees, angle being open on extensor surface. Refractured (ether) and dressed in full supination. July 15, no union yet. July 20, some union. Examined, August 15, 1907. Slight radial deviation of hand, due to rachitic deformity, same as in other arm. Supination and pronation complete. Class II.

CASE 31.—George W. D., aged fourteen years. July 23, 1907. Children's Hospital. Right, lower third. Full supination. Examined August 29, 1907. Supination complete, pronation about 140 degrees. Class I.

CASE 32.—Dillman F., aged five years. June 21, 1907. Children's Hospital. Right; compound of ulna. Dressed in mid-pronation. Examined August 8, 1907. Supination not quite complete, pronation complete. Some callus over radius, and slight deformity to flexor surface. Functions perfect. Class III.

CASE 33.—Clark W. B., aged four years. July 29, 1907. Children's Hospital. Left; same forearm was broken two years ago. Dressed in full supination. Examined August 29, 1907. Both bones bowed slightly to radial aspect; rotation from full supination is good. Class II.

CASE 34.—John H., aged twenty-two months. January 13, 1908. Episcopal Hospital. Left, greenstick. Full supination. Examined February, 1908. Class I.

CASE 35.—Marcus D., aged sixteen years. April 14, 1908. Episcopal Hospital. Epiphyseal separation of radius and greenstick of ulna above styloid. Full supination. Examined October 28, 1911. Class I.

CASE 36.—Louis S., aged fourteen years. April 22, 1908. Episcopal Hospital. Left, lower fifth. Full supination. Examined June 2, 1908. Class I.

CASE 37.—Charles W. H., aged 18 months. January 4, 1909. Episcopal Hospital. Left, greenstick. Full supination. Examined March, 1909. Class I.

CASE 38.—Clara Y., aged nine years. February 10, 1909. Episcopal Hospital. Right, two inches above wrist. Dressed on Bond splint, in mid-pronation, there being no tendency to deformity. Examined October 28, 1911. Class I.

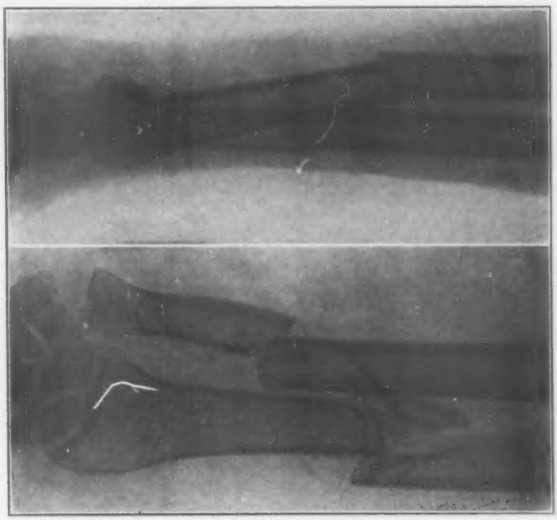

FIG. 9.—Case XXXIX. Lateral and antero-posterior views of comminuted fracture of both bones of forearm, showing best position secured. See Fig. 10.

CASE 39.—Michael S., aged fifty-three years. February 25, 1909. Episcopal Hospital. Right; comminuted; was caught in machinery. Dressed in full supination; accurate reduction not secured (Fig. 9). Delayed union. After ten weeks returned to his work (blacksmith), and two months later had firm union. Examined January 20, 1912. Right forearm: supination, 15 degrees; pronation, 105 degrees. Left forearm: supination, 0 degrees; pronation, 140 degrees. There is slight palpable bony deformity, but no disability whatever (Fig. 10). Class III.

CASE 40.—Victoria K., aged seventeen months. February 16, 1910. Episcopal Hospital. Right. Dressed in mid-pronation. Examined ten weeks later. Slight extensor bowing of ulna; supination and pronation complete. Class II.

CASE 41.—Wilson McC., aged fourteen years. March 23, 1910. Episcopal Hospital. Right, lower third. Full supination. Examined, January 20, 1912. No deformity palpable. Right forearm: supination, —35 degrees; pronation, 125 degrees. Left forearm: supination, —40 degrees; pronation, 140 degrees. Class I.

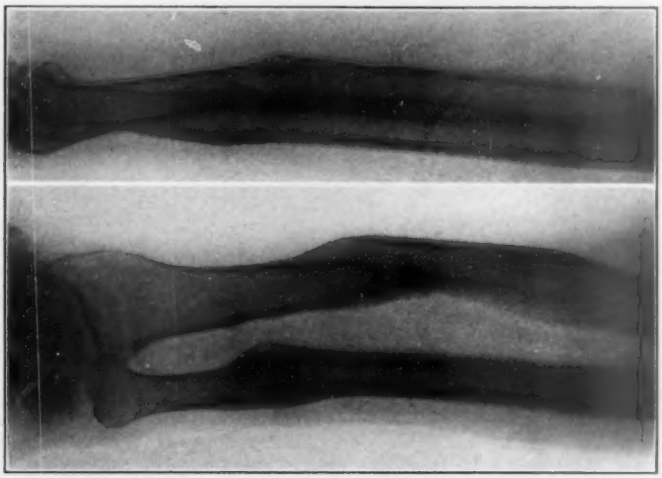

FIG. 10.—Case XXXIX. Lateral and antero-posterior views of comminuted fracture of both bones of forearm, three years after injury. There was delayed union, but patient was out of work only ten weeks in all. This is the worst result in the entire series.

CASE 42.—William E., aged fifteen years. January 18, 1911. Episcopal Hospital. Right, above wrist. Full supination. Examined October 28, 1911. Class I.

CASE 43.—Helen K., aged three years. January 28, 1911. Episcopal Hospital. Right, greenstick. Full supination. Examined October 28, 1911. Supination complete, pronation to 170 degrees. Class I.

CASE 44.—John L., aged seventeen years. August 11, 1911. Episcopal Hospital. Complete of radius, greenstick of ulna. Full supination. Examined October 28, 1911. Perfect result. Supination complete, pronation to 160 degrees. Class I.

CASE 45.—George S., aged nine years. August 11, 1911. Episcopal Hospital. Middle third, left; has been dressed in mid-pronation at another hospital. Examined October 27, 1911. Supination complete, pronation to 135 degrees. Class I.

CASE 46.—Harry M., aged thirteen years. August 16, 1911. Episcopal Hospital. Right, above wrist. Full supination. Ex-

amined October 28, 1911. Supination complete, pronation to 135 degrees. Class I.

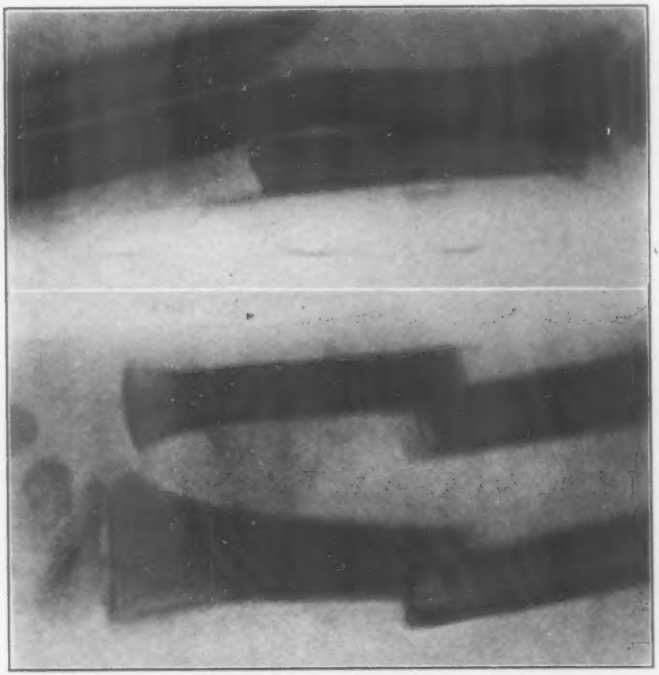

FIG. 11.—Case XLVII. Compound fracture of radius and ulna, before coming under care of the writers, and while still dressed in mid-pronation. See Figs. 12 and 13.

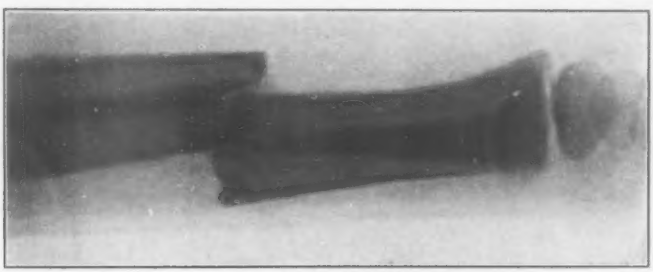

FIG. 12.—Case XLVII. Lateral view, after dressing in full supination, one week after injury.

CASE 47.—Roger McB., aged nine years. August 17, 1911. Episcopal Hospital. Injury one week ago, and was referred as suitable for operation; had been dressed in mid-pronation (Fig. 11).

Better position secured by dressing in full supination (Figs. 12 and 13), and no operation recommended. Compound fracture of radius and ulna, wounds on flexor surface of forearm. Examined January 20, 1912. Slight amount of callus palpable. Injured forearm: supination, —30 degrees; pronation, 130 degrees. Normal forearm: supination, —20 degrees; pronation, 135 degrees. Class II. (Fig. 14.)

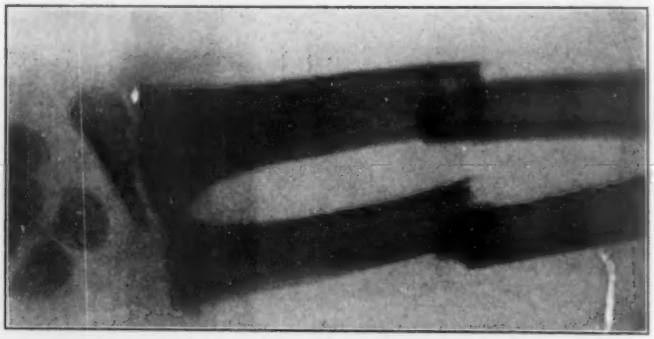

FIG. 13.—Case XLVII. Antero-posterior view after dressing in full supination.

FIG. 14.—Case XLVII. Compound fracture of both bones of forearm five months after injury. Slight callus palpable. No visible deformity. Perfect function.

CASE 48.—Tony M., aged fourteen years. September 8, 1911. Episcopal Hospital. Left; injury one week ago, junction of middle and upper thirds. Had been dressed in mid-pronation. Better position secured by dressing in full supination. Examined January 21, 1912. Slight posterior bowing of both bones. Left forearm: supination, 20 degrees; pronation, 150 degrees. Right

forearm: supination, —5 degrees; pronation, 140 degrees. Class II.

CASE 49.—Richard W., aged thirteen years. September 23, 1911. Episcopal Hospital. Left, middle third. Full supination. Skiagraph (Fig. 15) showed lower fragment of radius displaced

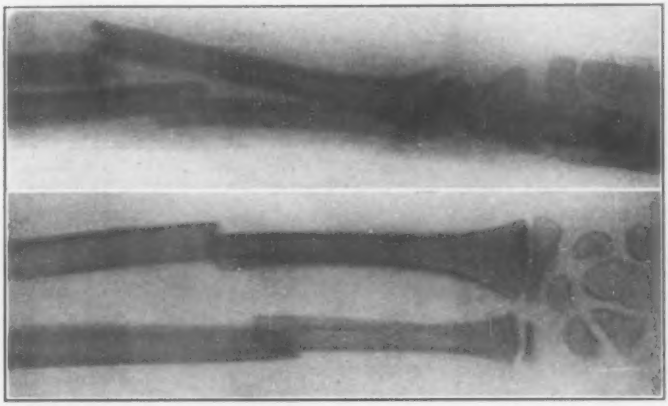

FIG. 15.—Case XLIX. Lateral and antero-posterior views after first dressing. See Fig. 16.

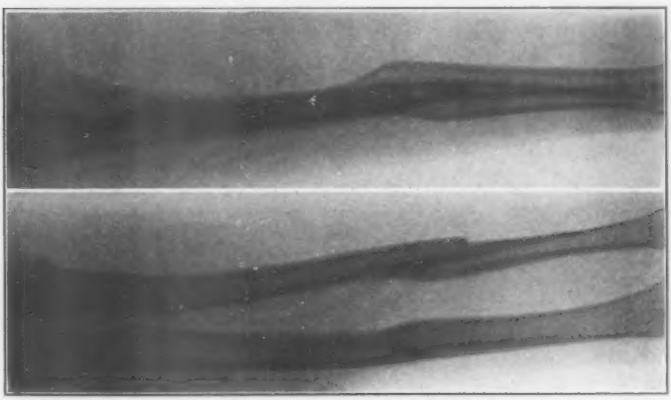

FIG. 16.—Case XLIX. Lateral and antero-posterior views four months after injury. Slight callus palpable. No visible deformity. Perfect function.

to flexor surface. Examined, January 17, 1912. No visible deformity, slight callus palpable on flexor surface of radius (Fig. 16). Left forearm: supination, —15 degrees; pronation, 125 degrees. Right forearm: supination, —10 degrees; pronation, 135 degrees. Class II.

CASE 50.—Herbert T., aged fourteen years. September 26, 1911. Episcopal Hospital. Right, middle third. Dressed in full supination. Examined January 21, 1912. Some callus palpable. Right forearm: supination, —10 degrees; pronation, 155 degrees. Left forearm: supination, —10 degrees; pronation, 140 degrees. Class I.

CASE 51.—John D., aged eighteen years. October 10, 1911. Episcopal Hospital. Right, junction of middle and upper third. Full supination. Some projection of upper fragment of radius on flexor surface. Examined January 28, 1912. Slight callus of radius. Right forearm: supination, 40 degrees; pronation, 135 degrees. Left forearm: supination, —5 degrees; pronation, 120 degrees. Class III. (This patient was under the care of the writers only seventeen days.)

CASE 52.—Stanley C., aged fourteen years. October 10, 1911. Episcopal Hospital. Left, lower third of radius, and through lower epiphysis of ulna. Full supination. Examined January 27, 1912. Left forearm: supination —15 degrees; pronation, 160 degrees. Right forearm: supination, —5 degrees; pronation, 160 degrees. Class I.

FURTHER EVIDENCE IN SUPPORT OF THE TOXIC PATHOGENESIS OF BRONCHIAL ASTHMA, BASED UPON EXPERIMENTAL RESEARCH.

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IN 1905, in a paper before the Orleans Parish Medical Society,[1] I called the attention of the profession to the importance of a consideration of the role played by intestinal toxins in producing various pathological conditions. Since then I have given the matter special attention, and I had already collected several cases of bronchial asthma, associated with intestinal toxins, which were relieved by abolishing the intestinal toxemia, when Rochester[2] read his paper in 1906, before the Section on Medicine of the American Medical Association. The discussion following this paper showed that the general opinion of the profession was opposed

[1] Proceedings Orleans Parish Medical Society, 1905.
[2] Jour. Amer. Med. Assoc., 1906, xlvii, 1983.

to the toxic pathogenesis of asthma. In 1909, before the Louisiana State Medical Society,[3] I reported several cases of bronchial asthma relieved entirely along dietetic lines by relieving the associated toxemia of intestinal origin; but discussion by Dock and others again revealed the fact that the profession was not as yet prepared to accept the toxemic basis of this symptom.

Since first becoming interested in the subject, I have collected histories of 121 cases of spasmodic bronchial asthma, partly my own and partly from other clinicians, which were associated with an intestinal toxemia, and were relieved by relieving this latter condition.

While I am not prepared, as yet, to claim that every case of asthma is due to a special toxin of intestinal origin and produced by the putrefaction of proteid material, I have yet to see one case in which, in my opinion, it is not the underlying cause.

Bouchard,[4] nearly twenty years ago, in speaking of paroxysmal attacks of asthma, states: "These, also, I suspect, we must rather consider the result of the elimination of toxic substances than a reflex act." However, in reading the literature pertaining to this so-called disease, one is struck by the various hypotheses expounded as to its etiology. Saenger[5] believes the underlying cause is an inherited "neurosis," with a mechanical obstruction superinduced by bronchial catarrh, and his treatment consists in relieving the latter condition by inhalations, etc.

Goldschmidt[6] also presupposes an hereditary neurosis, and classifies asthma into: (1) "Ein asthma epilepticum s. nervosum; (2) ein asthma bronchiale s. catarrhale paroxysmale; (3) ein asthma catarrhale chronicum; (4) ein asthma catarrhale permanens."

However, he recognizes: (1) "Ein asthma toxicum (aetiologische); (2) ein asthma catarrhale (anatomische); (3) ein asthma reflexivum (physiologische)."

He considers that the disease can best be classified according to its associated symptomatology, but in his toxic type he apparently considers that carbon dioxide poisoning of the blood stimulates the respiratory centre, resulting in the bronchial spasm, and does not mention the likelihood of intestinal toxins playing any important role. This view, to me, is untenable, after reviewing the recent work on the physiology of the respiratory centre carried on by Henderson[7] and others.

Bergmann[8] classifies asthma into: (1) A traumatic asthma, caused by stimulation of the respiratory centre through trauma to the cerebrum or medulla, as well as through a psychical defect

[3] Proceedings Louisiana State Medical Society, 1909.
[4] Lectures on Auto-intoxication in Disease, 1894, p. 171.
[5] Ueber Asthma und seine Behandlung, Berlin, 1910.
[6] Asthma, Munich, 1910.
[7] Johns Hopkins Hosp. Bull., xxi, 1910, 233.
[8] Das Asthma, sein Wesen und sein Behandlung, Wiesbaden, 1910, p. 36.

(2) A reflex asthma, caused by stimulation of the respiratory centre, through abnormalities in the various mucous membranes, as well as through a reflex stimulation of the respiratory centre through the central organism itself, as in so-called neurasthenia. (3) A toxic asthma, caused by the stimulation of the respiratory centre through the toxic condition of the blood.

Many other classifications are proposed, such as teeth asthma, supposed to be caused by defective teeth; dyspeptic asthma; and sexual asthma, especially advocated by Sadger,[9] a pupil of Freud.

The various classifications will continue to grow as long as we regard asthma as a distinct disease, instead of as a symptom of some other underlying constitutional condition.

The few reports of postmortem sections of patients dying in attacks of asthma, which I have been able to find in the literature,[10] are so widely at variance that no definite idea can be formed as to the pathology of this condition, further pointing to the fact that asthma should be classified as a symptom of an underlying constitutional pathological condition, associated sometimes with epilepsy, sometimes with cardiac disease, and at times, probably, with every disease known.

Hare[11] lays a great deal of stress upon the toxic basis of asthma, but his conclusions that it is brought on by "glycogenic distention of the liver," with resulting hypocarbonization of carbohydrates, is not based upon sound physiological facts, nor are his results in accord with my experience. More likely the engorgement of the liver of which he speaks allows the intestinal toxins to pass through into the general circulation without being synthesized, and their toxic action is thus manifested.

During the past summer and autumn, while working in Vienna with Prof. Karl von Noorden and Prof. Richard Kraus, I decided to attempt to prove or disprove our clinical deductions by animal gentlemen experimentation, and I wish to take this means of thanking these for their courtesy and assistance during my investigations and for their free provision of material.

The hypothesis put forward to prove was: "If asthma is caused by intestinal toxemia a definite toxin exists, which causes bronchial spasm similar in action to muscarin, and this toxin originates in the intestinal canal." In seeking this specific toxin, I was led to investigate the amins formed by intestinal putrefaction of the several amino-acids of normal pancreatic digestion of proteids, as I had long since satisfied myself by earlier chemical investigation and from the work of others, that the Charcot-Leyden crystals

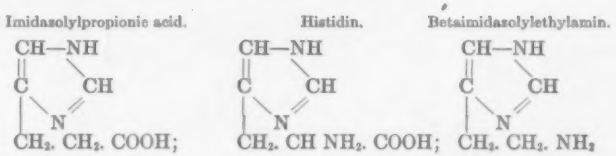
[9] Zentralbl. f. Psychoanalyse, 1911, Hefte 5 and 6, p. 200.

[10] Meeting held by the Militarärzlichen Gesellschaft, Berlin, 1886, p. 13; also see Berkast on Bronchial Asthma, its Pathology and Treatment, London, 1887; and Proceedings of the London Pathological Society, 1903.

[11] The Food Factor in Disease, London, 1905,

are amins closely allied to putrescin and cadaverin. On putrefaction the several amino-acids split off carbon dioxide and form their corresponding amins; so that we find a corresponding amin to leucin, tyrosin, arginin, histidin, and the other amino-acids formed in pancreatic digestion of proteids. The physiological action of the several amins have been excellently worked out by Barger and Dale,[12] and their results explain many of the clinical symptoms observable in cases of intestinal toxemia, although their work was carried on with a view to obtaining the active principles of ergot, adrenalin chloride, etc.

Of the several amins, betaimidazolylethylamin, while it has a slight action on the blood pressure, has a specific action on unstriped muscle tissue, causing contraction of the uterus as well as a contraction of the bronchioles, resulting in great dyspnea and death in the rabbit and guinea-pig, from complete occlusion of air by the tonic spasm of the bronchioles. The isolation of this amin and its physiological action was accidently discovered by Barger and Dale while investigating the action of ergot on the uterus. About the same time Kutscher[13] discovered a base in extract of ergot which had the same action on the bronchioles. Ackermann,[14] we find, was able to obtain the base by the putrefaction of histidin, while Windhaus and Voigt,[15] in 1907, were able to obtain it synthetically from imidazolylproprionic acid, according to the following steps:



Barger and Dale[16] were later able to obtain this base from an extract of the intestinal mucosa of the ox, indicating that the base is absorbed by this means from the intestinal canal. The experiments carried on by Dale and Laidlaw[17] to determine its physiological action were made with the base separated by them from ergot and from the intestinal mucosa, with the synthetic substance of Windhaus and Voigt[18] and with the base of Ackermann and Kutscher,[19] as well as with some of the base obtained by the putrefaction of histidin, the actions of which were all similar; so that their results can safely be accepted as representing the physiological action of betaimidazolylethylamin.

[12] Jour. Phys., 1910, xli, 1 and 2, 19.
[13] Zentralbl. f. Physiol., 1910, xxiv, 163.
[14] Zeit. f. phys. Chem., 1910, Band lxv, 504.
[15] Bericht des Deut. Gesellschaft, 1907, xl, 3691.
[16] Jour. Phys., 1910, xli, 494, No. 6.
[17] Ibid., 318, No. 5.
[18] Loc. cit.
[19] Zeit. f. Biol., 1910, Band liv, p. 387

Through the courtesy of Dr. Dale, I was able to obtain a large supply of the base for experimental purposes, and in this preliminary paper only a summary of the experimental work can be given, the details of which will appear in a later article, after a few further experiments have been completed. I obtained the identical results as Dale and Laidlaw,[20] namely, contraction of the uterus and bronchioles by intravenous injection, resulting in death from half a milligram in the guinea-pig, the animal dying in six minutes, with violent inspiratory efforts, the heart continuing to beat long after respiration had ceased. At post mortem the lungs were found pale and enormously distended and protruding from the thorax after section (Fig. 1). The spasm is so intense that when connected with a Meyer artificial respiration pump, no air can be forced in or drawn out of the lungs, the organ remaining permanently distended, as seen in anaphylaxis. In addition, I found that the same dose

FIG. 1.—Photograph of guinea-pig lungs after intravenous injection of 0.5 milligram of beta-imidazolylethylamin. Dark portions show normal lung tissue. Lighter portions are emphysematous.

administered into the trachea causes identical bronchial phenomena, while subcutaneous and intraperitoneal injections are much less toxic, suggesting that the action is entirely local on the unstriped muscle fiber and that the subcutaneous tissues have a detoxicating effect. Its action upon blood pressure and upon the uterus is not pertinent to the present subject, and I would refer anyone interested in this particular point to the paper by Dale and Laidlaw.[21]

Attempts so far to isolate the base from the blood of asthmatics have been unsuccessful, due to the many precipitations and filtrations; but experiments now in progress, I have reason to believe, will result in this being accomplished. However, I was able to

[20] Loc cit.

[21] Loc cit.

isolate the base by Kutscher's method from three specimens of feces, but was unsuccessful in twelve other specimens, suggesting that the presence of the base in intestinal contents will vary according to diet and probably also with varying intestinal flora.

Injections of the urine of asthmatics, as well as the urine of normal guinea-pigs and rabbits, cause the characteristic bronchial spasm and death, with the characteristic postmortem appearance of the lungs above referred to (Fig. 2). The appearance of the lungs and the symptoms of the animal are similar to those dying from an anaphylactic shock, recalling the opinion of Meltzer[22] that asthma is a condition of anaphylaxis. The delayed coagulation of the blood and the continuous fall of blood pressure observable in anaphylaxis is not found, however, after injections of betaimidazolylethylamin, although a lowered body temperature was uniformly observed.

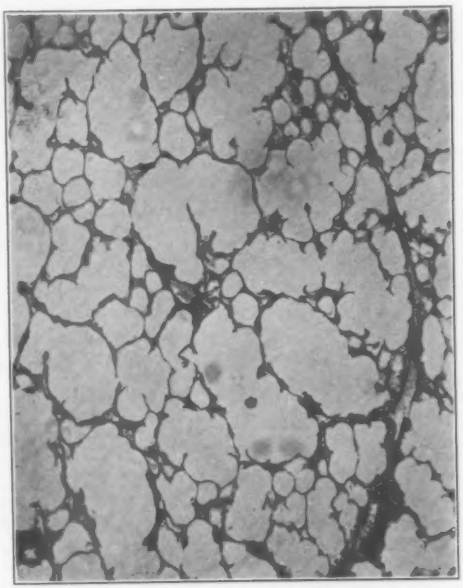


FIG. 2.—Photomicrograph of section of lung shown in Fig. 1. Note dilatation of air vesicles. 1 eye-piece and $\frac{2}{3}$ objective. × 87.

However, no one has as yet fully explained the phenomena of anaphylactic shock, and it is possible that in injecting a foreign serum a mixture of nitrogenous toxic bases is also injected, which

[22] Jour. Amer. Med. Assoc., 1910, lv, 1021–1024.

is ordinarily detoxicated, but which are not detoxicated by the tissues on the second injection of serum owing to the previous injection having exhausted this hypothetical detoxicating substance. From experiments, details of which will appear later, it appears that the normal human being, as well as the cat and dog, have the power of detoxicating not only betaimidazolylethylamin but also the other toxic amins formed by intestinal putrefaction, while the asthmatic individual has apparently lost this power.

We are accustomed to notice urticaria as evidence of intestinal toxemia, while the eosinophilia in asthma and anaphylaxis are frequent accompaniments of intestinal toxemia.

In my paper before the Louisiana State Medical Society in 1909, already referred to, I stated: "The fact that I have found evidence of auto-intoxication in every case of asthma examined by me for four years, leads me to believe that during the attack there is some toxin in the blood which acts similarly to the muscarin, or which depresses the respiratory centre to such an extent that the reflex stimulation of an inflamed nasal mucosa results in stimulation of the constrictor fibers of the vagus."

I now submit the above facts as bearing out, in part, my original contention, which I hope to be able to prove definitely in a short time by the isolation of this specific amin from the blood of asthmatics.

In closing, I wish to thank Dr. Maurice Couret, of the pathological department of Tulane University, for his kindness in taking the accompanying photographs.

A RECURRENT DISEASE OF THE SKIN ASSOCIATED WITH HIGH WINDS AND COLD WEATHER, FOR WHICH THE NAME DERMATITIS HIEMALIS HAS BEEN PROPOSED.

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The skin from its exposed condition is more influenced by extraneous conditions, such as climate, etc., than are other organs of the body. Many diseases of the skin are limited to certain

equatorial zones and others are greatly modified by climatic influences.

In 1874 Duhring[1] called attention to a pruritus, common in winter in certain regions of North America, which he called prurigo hiemalis. Hutchinson[2] and Hyde[3] have also emphasized the influence of climate in certain dermatoses.

The condition herein described first attracted attention in 1883, since which time many cases have presented themselves for observation and study.

A report on the syndrome as observed in 14 cases was read before the International Medical Congress in Rome, in 1894, by one of the present writers, and later in the year it was presented before the American Dermatological Association. In 1896 a second report was read before the International Dermatological Congress in London. Again, in 1902, a more complete investigation of the condition was made, 9 additional cases being reported and carefully studied, both macroscopically and microscopically, especially in regard to the possible parasitic causation of the disease, as well as the relation it bears to an ordinary eczema.

These studies may be summarized as follows: Dermatitis hiemalis is a cutaneous eruption having definite clinical symptoms, following a fairly uniform course, and always associated with or limited to cold weather. It resembles eczema in that there is an inflammation, watery exudation, and some itching. Unlike eczema, however, it more frequently is accompanied by smarting, burning, and tingling. It disappears during the summer months and reappears the following autumn. The seat of predilection is the back of the hands, wrists, and more rarely the fingers; very rarely the feet, and never the trunk, arms, or thighs. Again, unlike eczema, the lesions are circumscribed, well defined, often with elevated edges, with a tendency to heal in the centre. All symptoms are aggravated by atmospheric changes, especially by storms and sudden variation of temperature. The lesions are very resistant to treatment, although they disappear spontaneously at the approach of summer or when the patient goes southward away from the lake region. Occupation or sex appear to have little to do with the condition. Careful examination for saprophytic organisms has invariably given negative results. From clinical studies the affection appears to be more closely allied to some of the erythemas than to eczema, and may be similar to if not identical with the condition referred to by Jonathan Hutchinson[4] as "some peculiar eruptions allied to chilblains." Confirmatory is the suggestive bluish or purplish tint of the eruption that attacks the distal

[1] Philadelphia Med. Times, January 10, 1874.
[2] Clinical Lectures, London, 1879, i, 362.
[3] Chicago Med. Jour. and Exam., 1885, 1, 187, and 1886, 3, 116.
[4] Loc. cit.

extremities or parts farthest removed from the centres of circulation, and that it is met more frequently in the months in which there is the greatest variability in temperature. The histological findings are not distinctive, and the extent of the changes in the skin seems to be wholly dependent on the amount of the circulatory disturbances. This would lead one to infer that the disease is allied to eczema while characterized by some of the clinical features of chilblain. It presents, however, a distinct clinical picture which further observation may show is entitled to be looked on as a disease *sui generis*.

Since the presentation of the last paper many more cases have been observed, and we have made the following study, more especially on a few cases seen in the last two years. This work will be taken up under the following headings: (1) Etiology of the disease; (2) case histories; (3) a study of the histological findings, (4) the conditions of parakeratosis and acanthosis; (5) the course of pathological changes in the production of the disease; (6) treatment.

Etiology. At the International Medical Congress in Rome in 1894 it was questioned whether the etiological factor might not be found in one of the organisms of the tinea group, especially as the lesions were circumscribed and tended to heal in the centre. However, one of the writers, in conjunction with Dr. Henry S. Upson, presented a report on 4 cases before the International Dermatological Congress at London in 1896, in which it was shown that no pathogenic organisms were present. Moreover, such an etiological factor does not seem tenable, for if it were of parasitic origin it would undoubtedly affect other portions of the body and be carried from one person to another in the same family. This is not the case, for we have never seen 2 cases in the same family. Then, too, the affection is on an exposed part of the body which is very frequently cleansed, which again militates against the chance of such infection. Moreover, it occurs in winter, rather than in summer, a season unfavorable to the growth of organisms on exposed parts. During the past winter microscopic examinations of scrapings from several of the cases have been made, using ether to dissolve out the fat and a 10 per cent. potassium hydrate solution as clearing agent. In no case has any organism allied to the tinea group been found. Gram stains of the tissues in the latter stages of the disease have shown numerous gram positive skin cocci; but these, of course, are merely secondary invaders.

Having eliminated saprophytic organisms as a causative factor the influence of weather may be considered. Careful examination of the weather statistics for the last ten years shows that around the Great Lakes extreme daily variations in the thermometer are not any greater than in other parts of the country, for example, the inland cities of Cincinnati, Ohio, and Columbia, Missouri.

However, the weather is very variable, as may be easily shown. The average of the United States weather statistics for the last ten years shows that at Buffalo during the month of January, 14 per cent. of the days were rainy and 60 per cent. with snow, while 9 per cent. were foggy. There were also gales during 12 per cent. of the days and calms during 3 per cent. Cleveland during the same month had 13 per cent. of rainy days, 39 per cent. of snow, 4 per cent. of fogs, 9 per cent. of gales, and 6 per cent. of calms. During the month of March, averaged for ten years, Chicago had 24 per cent. of days with rain and a like percentage with snow, while 12 per cent. were foggy, 6 per cent. with gales, and 3 per cent. with calms. Buffalo during the same month had 22 per cent. of rainy days, 36 per cent. of snow, 15 per cent. of days with fog, 8 per cent. with gales, and 7 per cent. with calms. In Cleveland during the month of February the average for ten years shows the following: 13 per cent. of the days were rainy, 46 per cent. were accompanied with snowfall, 7 per cent. with fogs, 10 per cent. with gales, and 2 per cent. were calm days. These figures demonstrate the extreme variability of the winter weather about the Great Lakes.

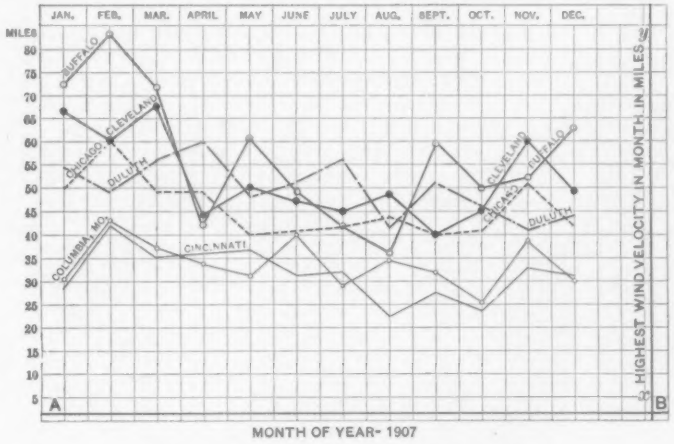


FIG. 1.—Highest velocity of wind in miles per hour.

In addition, this region is visited, especially during the winter months, with high winds. Examination of Fig. 1, taken from the report of the United States Weather Bureau for the year 1907, shows the highest velocity of the wind in miles per hour during the respective months, the lake cities, Buffalo, Chicago, Cleveland, and Duluth, being compared to the inland cities of Cincinnati, Ohio, and Columbia, Missouri.

It may be noted that the winds around the Great Lakes are especially high during the winter months and become somewhat lower during the months of June, July, August, and September. And not only are the winds of higher velocity in miles per hour, but examination of Fig. 2 will demonstrate that the total wind movement in miles per month is much greater in the cities of the Great Lake region than in the inland cities.

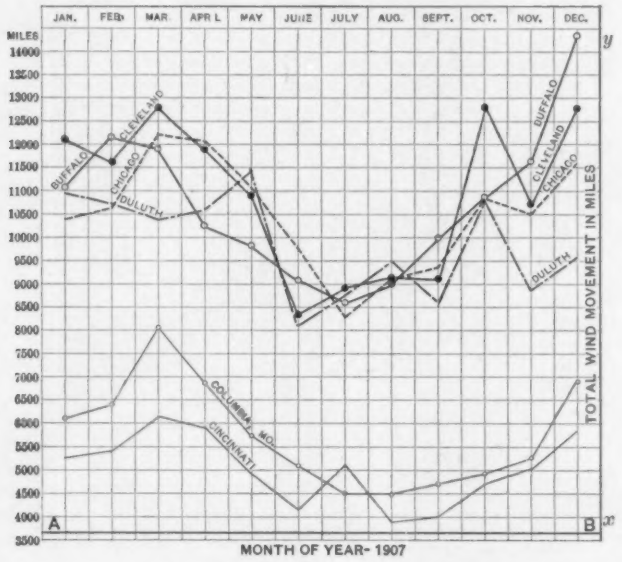


FIG. 2.—Total wind movement in miles per month.

To summarize, the winter climate around the Great Lakes, though not showing extreme changes in temperature in twenty-four hours, is very variable, especially in conjunction with the winds of high velocity and of high wind movement in miles per month.

CASE HISTORIES.

CASE I.—Female, aged twenty-three years; occupation housework. Aside from the present trouble the patient has always been well and strong. About two weeks before admission she first began to notice an itching, burning eruption which broke out on the back of one hand. Since then it has bothered her a great deal, and she has noticed a moist exudate at times. At the time of writing there is an area about 2 x 2 cm. on the back of the left hand, and a smaller one on the right wrist. Both areas are circinate, well defined, with

slightly elevated edges, and a tendency to heal in their centres. As yet there is verly little crust formation, but one sees some cracking of the surfaces and a little serous exudate. The areas are of a dark red color and show no induration. Patient says none in the family are troubled with a like affection, and she has never had it before.

CASE II.—George S., aged twenty-one years; switchman. The family and personal histories are negative. Patient had an infection of the second finger of the right hand three years ago, and ever since there has been a scaling and cracking of the skin over this area. About three months before admission an eruption broke out at the base of the third finger of the left hand and the like finger of the right. The lesions have extended a little, and a month later another lesion appeared on his right forearm. Patient was admitted to Lakeside Hospital for study. The blood showed at that time 3 per cent. of eosinophiles, otherwise nothing out of the ordinary was found. The lesions were similar to those of Case I except that there was crust formation and more induration of the areas. A biopsy was made of several fresh papules found on the affected area of the forearm. The finger involved for three years showed merely a chronic eczema, illustrating the fact that an eczema and a dermatitis hiemalis may be present on the same patient.

CASE III.—Carl W., aged thirty years; baker. Patient is a Bohemian, and was never troubled with this disease until last year, when he came to this country and settled in Detroit. The disease was present all winter, disappearing the summer following, only to appear again the next October. Patient came to Cleveland, hoping to be relieved of the trouble, but he has been troubled off and on for the last five months. The eruption itches and burns a great deal, and there is more or less of a moist exudation. The areas bleed quite easily; otherwise he feels perfectly well. Both posterior surfaces of the hands and one wrist are affected with well-defined, circinate, dark red lesions, showing an elevated edge and a noticeable tendency to heal in their centres. Crust formation is quite marked, and there is some induration of the parts. A biopsy was made of an area about three or four weeks old, and also from a spot of more recent appearance.

CASE IV.—G. W. P., aged thirty-five years; bookkeeper. His habits are good, and he has always been well, except for the present trouble. For the last ten years the patient has been bothered every year with an itching, burning eruption, which is limited to the hands, and is present only during the winter. It appears early or late in the fall, according to the severity of the weather, as he has himself noticed, and lasts until spring. At times the lesions will partially heal, but only to reappear, and he has never found anything that gave him much relief. He says he has never changed climate during the winter, so does not know what effect another climate would have on the condition. No others of the family are

troubled. The lesions on the back of the hands are quite extensive, but always well defined, and with a marked tendency to heal in the centre. The skin is quite thick, and there appears to be an hypertrophy of the upper layers. A biopsy was made of two areas of several months' duration.

It might be said that all the patients mentioned returned at more or less regular intervals during the winter. Their lesions would partially heal up at times, only to reappear, despite treatment. However, with the return of spring all of them immediately began to improve, and with the exception of Case III, all were well by the last of May. Case III reported himself well the middle of June.

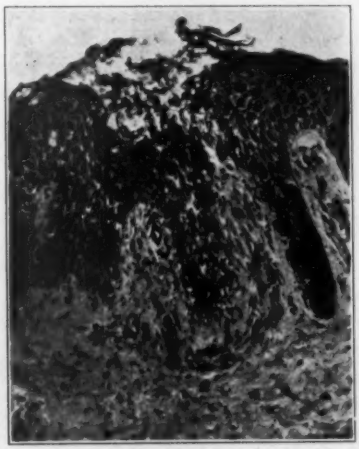


FIG. 3.—Early lesion. × 140. Bursting of a superficial vesicle, with marked edema and infiltration of the papillæ and epidermis with leukocytes.

A STUDY OF THE HISTOLOGICAL FINDINGS. A. *Early Lesion.* The lesion was taken from Case I. In the area of the section showing the least change from the normal (Fig. 3) we find the stratum corneum about 4 to 5 cells thick, in which the individual cells are made out with difficulty and most of the nuclei not at all. There is a stratum lucidum 1 or 2 cells thick in which the nuclei are absent and the cells are filled with fine granules. The stratum granulosum is 4 to 6 cells in depth and the cells show shrunken, hyperchromatic nuclei and masses of extruded chromatin in their protoplasm. The stratum spinosum under this is about 13 cells in thickness over the papillæ and 24 in the interpapillary processes of the epidermis. These cells are normal in appearance. The papillæ under this area show merely enlarged vessels with swollen endothelial cells and a slight perivascular edema. There is no perivascular cellular exudate.

A short distance from the area already described we come to a field where further changes have taken place (Fig. 8). Here the stratum corneum (*a*), about 5 cells thick, is made up of compressed, coherent cells; still containing their shrunken hyperchromatic

FIG. 4.—Moderately early lesion. × 120. Vesicle deep in the epidermis, with superficial crust formation. Stratum spinosum swollen and hypertrophied.

FIG. 5.—Height of process. × 70. Superficial crust formation and papillary vessel greatly dilated. Epidermis shows edema, acanthosis, and infiltration, with leukocytes.

nuclei. Intercellular spaces are seen between the lamellæ, probably filled with more or less fluid. The stratum lucidum (*b*) is scarcely discernible, and the stratum granulosum (*c*), 2 to 3 or 4 cells thick at one end of the figure, has nearly disappeared at the other end.

Still further changes are shown in Fig. 9, where neither the stratum granulosum nor lucidum are to be made out, and numerous small vacuolated areas are found under the lamellæ of the corneum. The latter, here 4 or 5 cells in thickness, still retains its nuclei and appears moderately lamellated. The prickle cell layer under this is from 13 cells in thickness over the papillæ to 28 cells in the interpapillary epidermis. The cells of the stratum spinosum over the papillæ are very much separated by edema, and about the middle of the stratum there is an area where the strain on the intercellular bridges has finally become so marked that they have broken, resulting in a vesicle formation, containing a few polymorphonuclear leukocytes, shrunken cells, and nuclei (Fig. 10). Deeper in

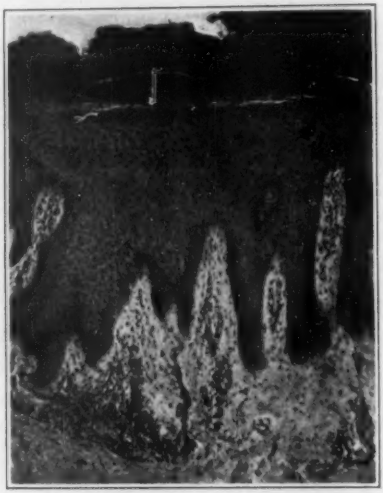


FIG. 6.—Chronic process. × 70. Intense parakeratosis and acanthosis. Marked leukocytic infiltration around the vessels of the corium.

the epidermis, between the papillæ, the edema is not so marked, and the cells are merely more or less separated. The edema is mostly extracellular in type. The papillæ in the region are very edematous, the vessels are enlarged, and their endothelial cells swollen, while there is an exudate of cells and fluid which have extended, not only into the papillary tissue, but also outward between the cells of the nearby stratum spinosum. The cellular exudate is mostly polymorphonuclear, with a few small mononuclears; indicating an acute process. The deep corium reveals little outside of a like condition around the vessels. There is no change in the collagen or elastic fibers.

B. *More Advanced Lesion.* This section was removed from an old lesion on the arm of Case II, as a few new papules had formed on it. Only the fresh lesion will be described.

At about the centre of the section (Fig. 4) there is quite a perceptible elevation of the epidermis. One notices at once the heavy edema and cellular exudate in the immediate vicinity. The stratum corneum consists of only 2 or 3 strands of flattened, nucleated cells which have been forced apart, as it were, by some pressure from below. Beneath them there is an open area dipping down into the epidermis, which contains mostly red blood cells, coagulated fibrin, and a few fragments of broken down epidermic cells. From this ruptured vesicle definite intercellular spaces lead down to the edematous papilla, although the spaces are clogged with an exudate

FIG. 7.—Healing process. × 70. Old crust on new-formed normal stratum corneum. Acanthosis of epidermis. Infiltration and thickening of vessels of corium.

of leukocytes and red blood cells. There is no stratum granulosum or lucidum and the stratum spinosum is about 8 cells thick over the papillæ and 16 to 18 cells thick over the interpapillary spaces. There is a marked general extracellular edema of the stratum spinosum, very few mitoses are seen, and the deeply staining nuclei are somewhat shrunken from their cell boundaries.

Corium: The papillæ in the area involved show enlarged vessels, with swollen endothelial cells. There is a marked edema of the perivascular tissue and a cellular exudation, mostly of polymorphonuclear leukocytes and red blood cells. The collagen fibers are swollen and stain poorly, while the nuclei are few and compressed. Elastic fibers are very fine. The vessels in the deeper corium will not be described at this time as they show the same results as observed in the older processes.

C. *Intermediate Stage.* In a stage slightly more advanced than the last, found in a section of tissue from a patient suffering from this particular lesion for two weeks, the following is noted: At one end of the section there is a large crust replacing the stratum corneum, and even thicker than the epidermis, being made up of coagulated fibrin, broken-down cells and nuclei, red blood cells, and numerous large gram positive skin cocci. Here and there one or two cells with shrunken nuclei and a partial extrusion of chromatin show us what should be the stratum granulosum. The stratum lucidum is absent. The stratum spinosum is about 12 cells thick over the papillæ and about 18 cells in thickness in the interpapillary epidermis. It gives one the impression of being swollen, which is accounted for by the marked intercellular edema,

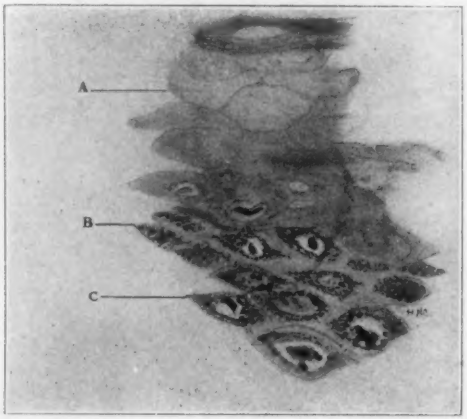


FIG. 8.—Earliest lesion, showing normal process of cornification. Superficial area of middle of the epidermis of same section as in Fig. 3. *A*, stratum corneum; *B*, stratum lucidum; *C*, stratum granulosum. All drawings—Figs. 8 to 12—were made with a Spencer camera lucida, Leitz 4 ocular and Leitz 12 objective, giving a uniform magnification of 1575 diameters.

while at one area there is a deep vesicle formation, in which coagulated fibrin, broken down cells, nuclei, and red blood cells are seen. Some of the red cells are noticed to have travelled out between the intercellular spaces of the stratum spinosum, the cells of which appear to be larger and better nourished than normally. Numerous mitotic figures are seen and several amitotic divisions are observed (Fig. 11), a very unusual condition, indicating the rapid multiplication of the cells. The vessels supplying this portion of the section are dilated, giving indication of a large vascular supply to the part. In addition to the changes already described in the previous sections a larger proportion of small mononuclear cells are present in the perivascular exudate, indicating a beginning chronic process of inflammation. At this stage the collagen fibers are beginning to

stain poorly, and they are forced apart by the edema of the tissues. No nerve tissue is observed.

D. *Height of the Process.* This is shown in a section of tissue from the same patient, but it exhibits a more marked change. It was removed from the posterior surface of the left hand.

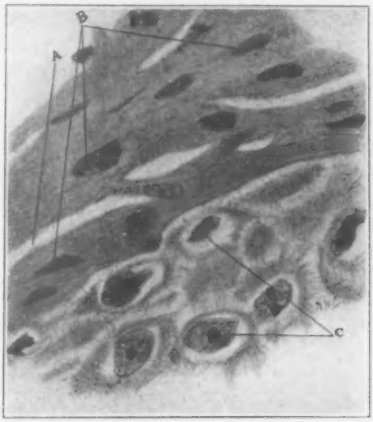


FIG. 9.—Earliest lesion, to show absence of stratum granulosum stratum ludicum. *A*, interlamellar vesicle formation; *B*, slightly hyperchromatic, persistent nuclei of lamellated stratum corneum; *C*, persistent stratum spinosum.

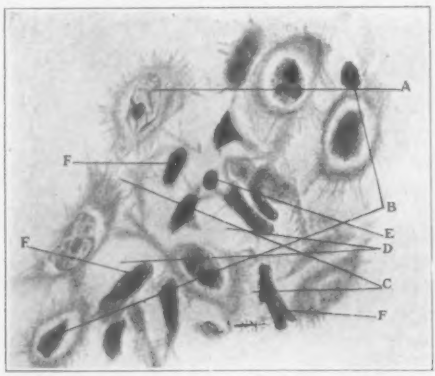


FIG. 10.—Early lesion. Superficial vesicle of prickle-cell layer below Fig. 4. *A*, normal prickle cell; *B*, shrunken nuclei of cells with intracellular edema; *C*, extracellular edema; *D*, vesicle formation; *E*, lymphocyte; *F*, shrunken nuclei.

On examination with the low power one is immediately struck by the heavy vascular supply of the parts (Fig. 5). A large crust extending nearly the entire distance across the section is made up of the same elements as the crust already described. There is no

stratum granulosum or stratum lucidum, but rather vacuolated areas filled with fibrin and more or less cellular exudate. Definite intercellular spaces lead down through the edematous prickle-cell layer to the very edematous, injected papillæ. These spaces are clogged with red blood cells and polymorphonuclear and small mononuclear leukocytes. The stratum spinosum is 6 to 8 cells thick over the papillæ and from 35 to 40 cells in thickness in the interpapillary epidermis. It is made up of large swollen cells showing numerous mitoses, the cells being separated more or less by edema. However, the edematous condition is more marked above the papillæ. These have an intense vascular supply and a perivascular edema that has entirely separated the tissues. The latter shows a very large cellular infiltration. The vessels in the deeper corium show a like condition, and there is a slight thickening of their walls, now and then a young fibroblast being seen. The collagen and elastic fibers show no changes not already described. No nerve tissue is seen.

E. *First Stage of the End Process.* This section to be described was removed from a chronic hypertrophied area from the hand of Case IV.

Examination even with a low-power lens shows a marked thickening of the stratum corneum and a great depth to the interpapillary epidermal processes. Near the centre of the section the following condition is observed: There is a stratum corneum (Fig. 6) about 40 to 45 cells in thickness, made up of flattened, incompletely dried-out cells in which the shrunken, hyperchromatic nuclei are still present. The stratum spinosum is about 35 to 40 cells thick between the papillæ and 10 to 12 cells thick over them. A layer of 2 or 3 cells showing a defective extrusion of chromatin from their shrunken nuclei gives evidence of a beginning formation of the stratum granulosum. There is no edema of the epidermis and no infiltration with cells. A few mitoses are seen, indicating a slightly increased nutrition of the part. The corium shows nearly the same condition as in the former section, and the type of cellular exudate around a papillary vessel is shown in Fig. 12. But at this stage the vascular supply is not so extensive and the vessel walls show some thickening, occasionally a young fibroblast being seen.

F. *Final Stage of the End Process.* This section is from an area on the hand of Case IV, and is of several months' duration (Fig. 7).

There is a stratum corneum about 12 cells thick, in which the outlines of the cells can still be made out, though with difficulty, and the nuclei exist only as empty spaces, having lost all their chromatin. Near the centre of the section there is a large dense crust, as thick as the horny layer, and superimposed upon it. There is a nearly normal stratum granulosum 3 or 4 cells thick and a stratum lucidum 1 or 2 cells in thickness. The prickle-cell

layers shows a definite acanthosis from the long-increased blood supply, and is about 15 cells in thickness over the papillæ, and from 30 to 32 cells thick between them. There is very little intercellular edema and none intracellular. The cells are large, and appear to be well supplied with nourishment, and one amitotic

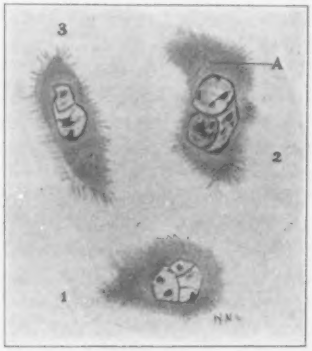


FIG. 11.—Moderately early condition, from portion of same area as Fig. 4, and showing cell division by amitosis. *A*, beginning vacuolar degeneration.

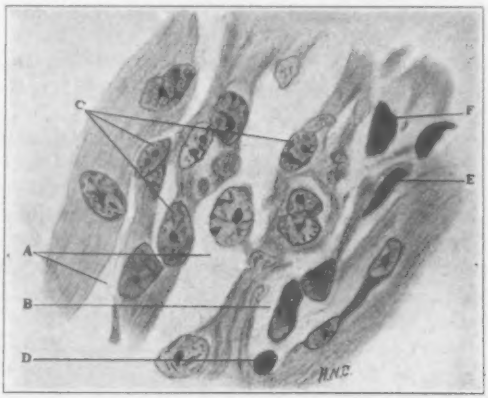


FIG. 12.—Chronic process. Portion of middle of papilla from same area as Fig. 6. *A*, dilated vessles; *B*, perivascular edema; *C*, swollen endothelial cells; *D*, lymphocyte; *E*, shrunken nucleus; *F*, large mononuclear cell.

division is observed. The vessels of the papillæ are still moderately dilated and have swollen endothelial cells. Still there is very little exudation of serum and only a few perivascular elements, mostly small mononuclears and young fibroblasts. The collagen fibers of the corium are still swollen and forced apart, but they are beginning to stain more readily. The elastic fibers are fine and not

forced apart so much as in previous sections. No nerve elements are seen. The vessels of the corium show thickened walls and swollen endothelial cells lining them, while a few young fibroblasts are seen in the walls. Their intense perivascular exudate is mostly small mononuclear cells and a few young fibroblasts; now and then an eosinophile is seen.

Production of the Conditions of Parakeratosis and Acanthosis. Before taking up the study of the course of events in the different stages of this condition it may be well to review the subjects of parakeratosis and acanthosis somewhat in detail, especially as they have an important bearing on the findings of this condition in its different stages. As already emphasized by Corlett and Schultz,[5] "cornification is not a process of specialization and differentiation but of gradually progressing physiological degeneration, which leads ultimately to death." Apparently the only functions preserved by the epidermal cells are nutrition and multiplication, and as they get further from their papillary blood supply they lose first their power of multiplication and later that of nutrition. The cells then begin to dry up and their nuclei shrink and become hyperchromatic. This nuclear chromatic material is then partially extruded from the nucleus, from disturbance of the cell-nucleus balance, resulting in the coarsely granular cells of the stratum granulosum. Later it is entirely extruded and finely distributed through the protoplasm, while the nucleus disappears entirely, cells of the stratum lucidum type. In the final death of the cell the chromatin disappears entirely and the cells of the stratum corneum are mere dried up, horny lamellæ.

However, if there is an edema of the tissues with resulting increased nutrition of the epidermal cells, we will find a disturbance in the process of cornification. The cells not only are able to multiply for a longer period than normally, but they retain the power to assimilate nutrition and fluid. Consequently, they do not become dried up until they reach the surface, so that no cells of the stratum granulosum or stratum lucidum type are formed. At the surface the rapid, only partial drying-out process results in the formation of nucleated, horny lamellæ. All variations between this condition of parakeratosis and the normal may be found, depending on the degree of edema of the parts.

The phenomena of acanthosis are likewise dependent in part on the increased nutrition of the cells. As Unna[6] has already pointed out, in the normal epidermis from one-fourth to one-third of the epidermal mitoses takes place in a middle zone of the stratum spinosum and from two-thirds to three-fourths in the two lower layers of cells of the epidermis. But in a condition of edema where

[5] Jour. Cutan. Dis., February, 1909.

[6] Die Histopathologie der Hautkrankheiten, Berlin, 1894, s. 204.

all the cells are bathed in an increased nutritious serum, they retain their multiplicative and assimilative capacities longer than usual, and we find many mitoses, even but a few cells deep from the external surface. Consequently, more cells are formed, they are larger, and live longer than normally. Hence the epidermis is thickened, and is found not only to extend further upward, but the interpapillary processes even extend deeper into the corium, and we have acanthosis.

THE CHANGES OBSERVED IN THE PRODUCTION OF THE LESIONS. We are now ready to explain the course of events in the production of the lesions. Given a susceptible person the variable, wintry, windy weather, as met with in the Great Lake region of North America causes an irritation of the skin of the hands, resulting first in a slight vascular dilatation of the vessels of the papillæ. The endothelial cells lining the vessels swell up, and if the condition continues there will result the extravasation of some serum from these vessels into the papillary tissue. Possibly a few polymorphonuclear leukocytes will also find their way into the surrounding tissues. The irritation still continuing, there will be a constantly increasing vascular dilatation, and a larger amount of serum being poured out, it will gradually work out through the lymph channels of the epidermis, resulting in a higher or lower grade of edema. And, as has been shown, even a slight grade of edema will exercise quite a marked influence on the process of cornification, resulting in a parakeratosis. The process of exudation of the serum from the papillary capillaries, with the passage out of leukocytes and red blood cells, may be very rapid in its course. Then this exudate, working out from the papillæ, through the lymph channels into the epidermis, may cause such a sudden strain on the intercellular bridges of the prickle cells that they are no longer able to withstand, and they burst. Such a condition we find in Fig. 10, when the vesicle is deep in the stratum spinosum. However, suppose the edematous area is situated high up in the epidermis and that the area is covered only by a few layers of rapidly and incompletely cornified cells. Then when the pressure becomes too great the vesicle may break outward and we find such a picture as is shown in Fig. 3, the vesicle containing fibrin, broken-down leukocytes, and red blood cells. Such an exposed area is soon changed into a crust of coagulated serum, broken-down epithelium, nuclei, red cells, and leukocytes. This is the height of the process, and at this time we almost invariably find a secondary growth of Gram-positive skin cocci in the crust. There are also more or less changes in the deep corium, due to the etiological factor before mentioned, in connection with the irritation of broken-down cellular products, etc. Here, too, the vessels become dilated, the endothelial cells swollen, and an exudate of serum and polymorphonuclear cells is poured out into the surrounding tissues, resulting

in a perivascular edema and inflammation. Indeed, the perivascular edema may be so marked at this time that the tissues are entirely forced apart and broken up.

Again, suppose the irritation has continued for some time, then we will find an even more severe type of change around the vessels of the corium. There is a heavy exudate of serum and leukocytes, the latter mostly small in type, with an occasional eosinophile and endothelial cell. The collagen fibers are swollen, forced apart, and stain poorly, while their nuclei are flattened from the pressure of serum in the tissues. The elastic fibers are also forced apart. The result of the copious supply of serum from the papillary vessels to the epidermis is that the cells receive better nutrition than normal, so that they are continually bathed in serum. Instead of drying up they will continue to assimilate nutrition and to multiply, both by direct and indirect division. The result is the production of a thickened epidermis, showing an atypical process of cornification, parakeratosis. Moreover, examination shows us long interpapillary processes of epidermis made up of large, healthy looking cells, showing numerous mitoses and apparently growing down into the corium as well as upward, acanthosis. This is the intermediate step between the acute and the chronic process as shown in Fig. 6, Crusts may or may not be present.

As the chronic stage begins to appear we find certain vascular changes that have a very important bearing. From the long-continued irritation we not only have the perivascular exudate already spoken of, but, as in Fig. 12, the vessel walls become thickened and a few young fibroblasts are seen in the walls and in the surrounding tissues. This thickening of the vessel walls tends to reduce the blood supply and consequently the edema, so that once more we have a return of the tissues to the normal, from the decreased vascular supply. Such a condition is shown in Fig. 7, where a thickened, evidently long-irritated epidermis is shown undergoing a normal process of cornification, though it still retains a crust above it, revealing an old process as yet incomplete.

Either the healing takes place through a process of chronic inflammation, as outlined above, or at the approach of spring the changeable, windy weather no longer irritates the susceptible parts, so that even though the process be acute, by removing the causative factor the condition tends to subside from lessened blood supply, and thus a return to the normal is found.

Treatment. Of this little need be said, as no treatment seems to have much effect, at least not for any length of time. The general hygienic care of the skin should be enjoined, together with such protective measures as the wearing of leather gloves, etc. No special internal medication has been found of any avail. Locally, diachylon ointment with salicylic acid, varying in strength from 3 to 10 grains to the ounce, may be used, often with good results for

the time being. At times, Lassar's paste seems to work well, while the boric acid ointment (U. S. P.) or the white percipitate ointment, 5 per cent., may be used. As a prophylactic to those predisposed simple protective applications of petrolatum and paraffine are indicated on the approach of cold weather. In all cases the patient should be cautioned to keep the hands out of water as much as possible, and to avoid all local irritants. The ideal treatment to be advised is a change of climate to a warmer region, a treatment always followed with a disappearance of the trouble.

In conclusion we wish to thank Dr. O. T. Schultz, of the Pathological Department of the Western Reserve University, for his valuable assistance and suggestions in the histological study of this paper. To him also thanks are due for the taking of the photomicrographs.

EXPERIMENTAL STUDY OF THE EFFECTS OF URETERAL OBSTRUCTION ON KIDNEY FUNCTION AND STRUCTURE.[1]

By Edwin Beer, M.D.,
NEW YORK CITY.

The following work was begun over four years ago, to determine, if possible, how long a ureter might be tied off, before making an ureterovesical anastomosis, without sacrificing the involved kidney's functional integrity. In the course of difficult pelvic dissections it is well known that the ureters are occasionally injured and at times the attempt to repair the damage protracts the original operation to a dangerous degree. To avoid this prolongation, numerous operators have resorted to direct ligation of the involved ureter[2] above the point of injury, relying upon the natural process of atrophy to take care of the thus excluded kidney. If an operator is thus forced to exclude the kidney of one side, either actuated by such doubts as are engendered by undue prolongation of the operation, or by reason of the fact that the operative technique appears to be too difficult, the possibility of a later operation anastomosing the excluded side with the bladder has been completely ignored, so far as I have been able to discover in a study of the literature. To determine how long such a kidney could wait without losing its functional adequacy was the original impulse for this study, in the course of which many other interesting points developed. In this paper I expect, therefore, as briefly as possible,

[1] Read before the Surgical Section of the New York Academy of Medicine, 1912.

[2] L. Landau, Deut. med. Woch., 1900; Wassiljew, Deut. Zeit. f. Chirurgie, 1907, lxxxix; A. V. Rosthorn, Jour. Amer. Med. Assoc., 1906, p. 1881.

to bring all these facts together without extensive narration of numerous experimental details involved.

All the work was done on some 60 dogs in the surgical research laboratory of Columbia University. To the gentlemen in charge of this laboratory, as well as the students who assisted me, I owe a debt of gratitude, which I gladly take this opportunity to express.

I. Hydronephrosis May Result from Infection of the Ureteropelvic Tract Without Stenosis. A series of experiments was made with the object of determining the effect of direct injection of cultures into the ureter after extraperitoneal exposure of the same without in any way injuring its lumen by artificial stenosis. Colon bacilli were injected through a fine needle. The involved kidney and ureter were removed at varying times, and regularly showed well-marked hydronephrosis and hydroureter. In the earliest case the kidney was examined nine days after the injection, and the organ was enlarged and the pelvis moderately dilated. In another case, after fourteen days, the kidney was removed and it was practically normal, except for well-marked hydronephrosis. In another case, after twenty-one days, a good-sized hydronephrotic sac was present.

In none of the cases were abscesses produced in the kidney parenchyma.

II. Hydroureter and Hydronephrosis of an Extreme Degree, in Time Leading to Complete Parenchymatous Atrophy, Follow Injection of Infectious Organisms Above a Stenosis. If the same technique is followed as was used in Group I plus complete or incomplete ligation of the ureter, whether with *catgut* or with *silk*, an extreme degree of distention of the pelvis and ureter follow, unless the injected bacteria are too virulent, when pyonephrosis or pyelonephritis and early death follow. The early pictures are very much as in group I. Thus already in five days a moderate hydronephrosis has developed. In another case in eleven days there was a marked dilatation with some perinephritis. In another in twelve days, the same picture. In cases lasting thirty-five days a very large hydronephritic sac developed despite the use of a catgut ligature in producing the stenosis. In still another case, after fifty-six days, nothing but a large sac was left representing the destroyed organ.

III. After Developing a Primary Hydroureter and Hydronephrosis of a Mild Degree, the Kidney Undergoes Atrophy if the Ureter is Tied and no Infection is Superadded. If the same technique is used as in group II, and no organisms are introduced into the ureter, there is a primary dilatation above the stenosis, which gradually recedes after the first two or three weeks, and then the pelvis becomes folded on itself and the kidney parenchyma gradually atrophies. This atrophy becomes so complete that at the end of five months (Case 9) the excluded kidney is

nothing more than a firm fibrous mass, measuring from pole to pole one inch and from sinus to convexity one-half inch, with folded enlarged pelvis and ureter. These phenomena are of importance in connection with the problem which led to this series of experiments, as they bear upon the essential question that is involved, that is, the functional adequacy of an excluded kidney.

FIG. 1.—Normal kidney with slit-like pelvis.

FIG. 2.—Atrophic kidney, three months after ligation; no infection.

From this series of observations it seemed likely that the excluded organ was able to secrete up to about the third week as evidenced by the dilatation and distention of pelvis and ureter up to this date. It also appeared that after these three weeks the function was materially impaired as the distention, probably an evidence of secretory activity, disappeared. Chemical examination of the fluid in the distended ureter showed varying amounts of urea, which seemed corroborative of this view point. Fluid removed three weeks after ligation showed no urea in one case; in another, twenty-four days after ligation, only 0.005 gram per cubic centimeter, whereas fourteen days after exclusion in another case the urea was as high as 5 per cent.

IV. IF A KIDNEY IS EXCLUDED UP TO THREE TO FOUR WEEKS AND THEN ITS URETER IS REIMPLANTED IN THE BLADDER, THE KIDNEY SEEMS CAPABLE OF CARRYING ON ALL THE EXCRETORY

WORK OF BOTH ORGANS. To adequately test the functional capacity of the reimplanted kidney, it was necessary to remove the other kidney. Cystoscopic examinations with indigo carmine, though repeatedly made, I did not accept as conclusive evidence

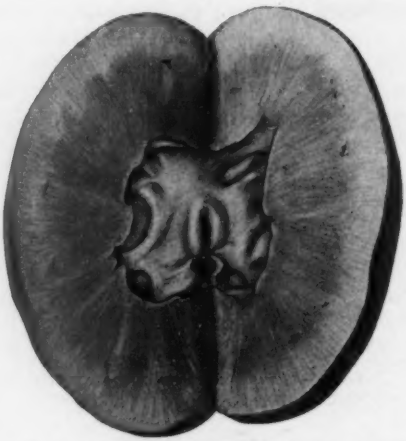


FIG. 3.—Two weeks after ligation plus infection (hydronephrosis).

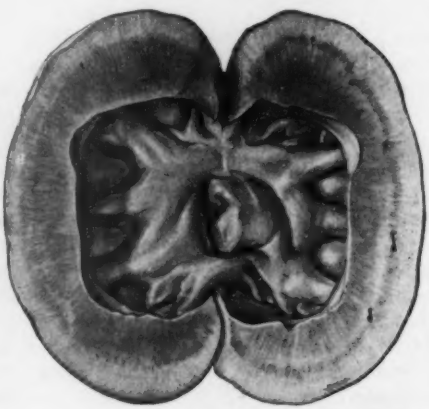
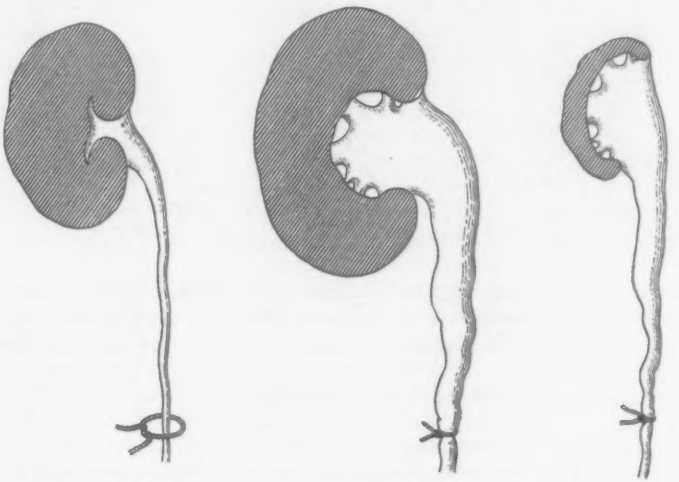


FIG. 4.—Four weeks after ligation of ureter plus infection (hydronephrosis).

of renal adequacy or inadequacy. Consequently the most exacting test was resorted to and nephrectomy of the second organ performed. In human surgery we will not be called upon to perform any such test, nor is such a degree of adequacy required. If one can reimplant an excluded kidney that has only 50 per cent. of

the total renal capacity it is that much gain, as all cases coming into this category must have a second adequate organ.

FIG. 5.—No. 226. Exclusion of three weeks. After nephrectomy of the other organ animal lived on this kidney until the ureter became plugged with a calculus, almost two months after removal of second kidney.



Normal kidney. Three weeks after ligation. Three months after ligation.

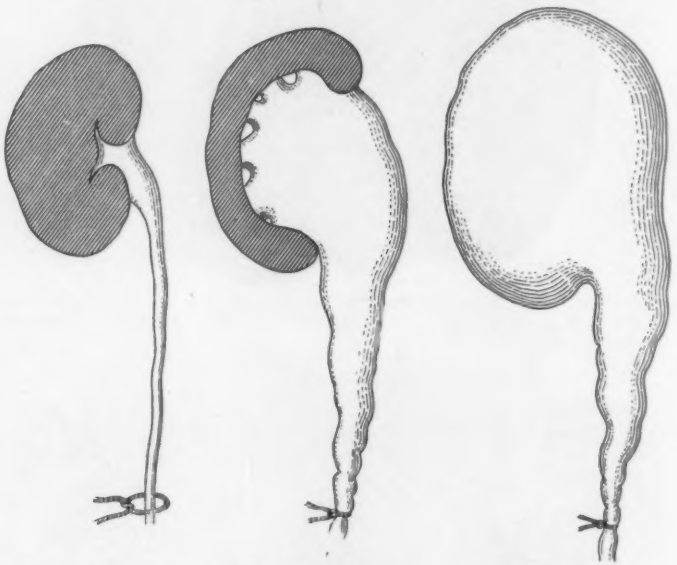
FIG. 6.—Aseptic series.

To demonstrate the evidence upon which the conclusions just mentioned are based, I shall report several experiments in detail. The accompanying drawings, Figs. 1 to 7, from specimens, together with the diagrams, illustrate well the processes just described.

Experiment. (215) Male dog.

March 24, 1909. First operation. Through low laporatomy the right ureter was exposed at insertion into bladder. Silk ligature tied at this point.

March 31, 1909. A low left-sided Kammerer incision. Bladder drawn into wound after separating omental adhesions. The



Normal kidney. Three weeks after ligation. Three months after ligation.

FIG. 7.—Septic series.

ureter was found dilated moderately with clear amber-colored fluid. An anastomosis of ureter and bladder was made, side to side, by means of a silk ligature (McGraw technique), reinforced with Lembert sutures.

April 24, 1909. Dog in fine condition

May 29, 1909. Left lumbar nephrectomy.

September 1, 1909. Dog died.

Autopsy. Bladder contains amber-colored fluid; specific gravity 1024; urea 0.2 per cent.; alkaline; microscopically, many pus cells and inorganic salts. The pelvis of the kidney and ureter contain mucopus full of gravel. The parenchyma shows numerous abscesses.

The pelvis is dilated. The new opening in the bladder is surrounded by edematous tissue, which has stenosed it, preventing ready emptying of distended ureter into bladder.

Remarks. In this dog the right kidney was excluded for one week and then the corresponding ureter was implanted in the bladder. After the dog had thoroughly recovered from these operations the adequacy of this kidney was tested by removing the left kidney. The dog continued to live for over three months, showing no signs of renal insufficiency. Had not infection supervened death might not have resulted when it did. In brief, this dog's right kidney, though it had been excluded from work for seven days, was capable of carrying on all the renal excretory work of the organism.

Experiment. (226). Male dog.

April 3, 1909. First operation. Right ureter exposed close to bladder by transperitoneal route, and ligated.

April 17, 1909. In excellent condition.

April 24, 1909. Three weeks after ligation of ureter the anastomosis between the dilated ureter and bladder was made by a double row of sutures. Cultures[3] from dilated ureter, which contained bloody turbid fluid, showed Staphylococcus albus.

May 8, 1909. Doing well.

May 22, 1909. Nephrectomy (left kidney).

June, 1909. Dog did very well.

July 11, 1909. Sudden development of anuria followed by death.

Autopsy. Calculus found plugging the ureter. Kidney shows dilated pelvis full of white calculi, one of which had wandered into and blocked the ureter, producing the fatal anuria.

Remarks. In this dog the kidney had been excluded three weeks before it was allowed to resume its work, and after this period it was still capable of doing the necessary excretory work. No signs of renal insufficiency developed until the accidental blocking of the ureter by a calculus took place.

Experiment. (38). Fox terrier.

August 16, 1909. First operation. Ligation of right ureter close to bladder.

September 15, 1909. Anastomosis of ureter and bladder thirty days after the first operation. Cultures showed Staphylococcus albus.

December 13, 1909. In good condition.

February 19, 1910. Nephrectomy (left kidney).

February 20, 1910. Doing well.

Urinalysis. Specific gravity, 1030; alkaline reaction; faint trace of albumin; 2 per cent. urea; phosphates and pus cells.

[3] I take this opportunity to thank Dr. H. Celler for the bacteriological examinations which he very kindly made for me.

February 21, 1910. Total urine gathered, 345 c.c.; specific gravity, 1020; alkaline; 1.5 per cent. urea.

February 22, 1910. Total urine gathered, 480 c.c.

February 23, 1910. Total urine gathered, 750 c.c.

February 27, 1910. Total urine gathered, 720 c.c.

March 5, 1910: Dog in excellent shape. Continues to take food well; no vomiting; active and growing fat.

March 19, 1910. In excellent condition.

April 8, 1910. Killed. Autopsy showed a large stone in bladder, three-quarters of an inch in diameter. New ostium patent. Right ureter somewhat dilated. Right kidney is approximately one-third the size of the previously excised left kidney, which had been removed February 19, 1910. It measures one inch in the vertical and one-half inch in transverse diameter.

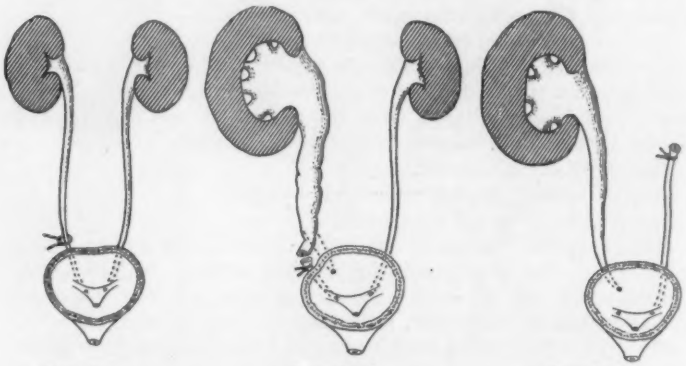


FIG. 8.—Series testing functional adequacy.

Remarks. This dog lived satisfactorily on the right kidney, which did all the necessary excretory work, even though it had been excluded for thirty days. In still another dog (Case 40) I excluded a kidney for thirty-seven days, and when it was tested by the same physiological test, that is, forced by nephrectomy of the second organ to do all the work, it excreted four days after the nephrectomy 650 c.c. of urine, which on testing was alkaline in reaction, contained a faint trace of albumin, urea 1.6 per cent. (10.4 grams). Subsequently this animal developed signs of insufficiency, and vomiting set in, followed by anuria and death.[4]

Resume. From such experimental data it is evident that even after three or four weeks exclusion of a kidney, sufficient parenchyma is preserved to carry on the excretory work of the organism. Whether these results in dogs can be transferred to humans,

[4] Fig. 8 illustrates the various steps taken to test the adequacy of the excluded kidney.

experience alone can tell us. The knowledge gained from these data are very suggestive and in future if an operator resorts to ligation of a ureter, he must bear in mind the fact that the excluded kidney may be made a useful organ if an anastomosis is made within three to four weeks of the original exclusion.

From the work done in connection with this subject, the following conclusions seem justified:

1. Infection of a non-stenosed ureter may lead to a hydronephrosis. Perhaps this explains some of the cases of hydronephrosis in which no mechanical cause is found.

2. Infection of the ureter rarely leads to abscess formation, to multiple abscesses of kidney, unless the ureter is stenosed and then only when the injected organisms are virulent.

3. Aseptic ligation of ureter leads regularly to a primary hydroureter and at about three weeks atrophy and shrinkage of the hydronephrotic sac begins.

4. The idea that the use of catgut ligature material in pelvic work will not cause a permanent ureteral stenosis, if this organ is tied off, is erroneous.

5. Three to four months after ligation of the ureter the kidney is represented by a small fibrous mass, provided infection is not present. If infection is introduced a huge hydronephrotic sac without vestige of parenchyma results.

6. In face of infection, stones readily form both in the pelvis and bladder.

7. After three weeks' exclusion sufficient parenchyma persists to warrant an attempt at secondary implantation of the ureter into the bladder.

THE USE OF THE CREHORE MICROGRAPH IN THE CLINICAL AND EXPERIMENTAL STUDY OF CARDIOVASCULAR PHYSIOLOGY.[1]

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AND

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(From the John Herr Musser Department of Research Medicine, University of Pennsylvania.)

In the last few months we have attempted to use the Crehore micrograph[2] for the study on animals of (1) the time relations of

[1] Read before the Philadelphia Pathological Society, May 9, 1912.

[2] Amer. Jour. Med. Sci., 1912, cxliii, 193.

the contractions of various parts of the heart, (2) the correlation of these with intra-auricular and intra-ventricular pressures, (3) the transmission time of pulse waves under various conditions, and (4) the time relations of heart sounds and of murmurs. Clinically we have tried to apply it to the study of the jugular pulse, of heart sounds and murmurs, and of the transmission time of the pulse waves. It has been impossible to complete any phase of the work, because in the use of the instrument we have met with constant difficulties. These have been for the most part of a technical nature, which could be met by some modification of the construction or by a sufficiently frequent readjustment of the instrument, but which are so numerous that for their correction an almost complete reconstruction of the instrument would be necessary. In addition to these minor difficulties there are some objections to the principle of the Crehore micrograph when applied to physiological studies. Some of our difficulties were as follows:

1. *The Tambours.* We found that upon testing our tambours they were not air tight. To render them so it was necessary either to seal the joint between the base of the tambour and the diaphragm, forming its upper surface, or to place some form of washer between these two. The instrument not having been constructed with a view to this change, neither operation has proved to be altogether simple, and, in fact, we have found it difficult to so adjust the instrument that when a given displacement on the receiving tambour is made and maintained there will not be a gradual return of the recording tambour toward the resting position. Such a defect, of course, renders the instrument useless for graphic registration.

Another unfortunate feature of the instrument is in the mirrors attached to the tambours. These mirrors are but lightly silvered. If they be too little silvered, not enough light will be reflected to give a good photograph; if, on the other hand, they be too heavily silvered, the interference bands are obscured and the record cannot be read. As the silvering undergoes oxidation in the air resilvering must be done from time to time, and no method has yet been devised for securing precisely the correct degree of silvering except that of repeated trial.

The adjustment of the interference surfaces is likewise a time-consuming operation. Once the interference bands appear it is a matter of no difficulty whatever to adjust them properly, but it is often a matter of minutes or even an hour or more before they can be made to appear at all.

2. *The Photographing Apparatus.* One of the most serious difficulties which we have encountered is the inadequate provision for securing an evenly moving film. Whether soft copper wire be used to draw the film holder along its track or steel wire, which is less prone to kink, the movement of the film is far from even.

This is shown by the use of some type of time-marker, and also by the alternately darker and lighter zones across the film due to varying lengths of exposure as the rate of the film changes. Such a defect, of course, renders accurate time measurements impossible.

Another defect is the limitation in both directions as to the speed that can be chosen for the film. As noted above, the mirrors must not be too highly silvered or the bands will be obscured. This means that the intensity of the light reaching the film is limited, and in turn the rate of the moving film must be kept below a certain speed in order to secure sufficient exposure. On the other hand, if the film is propelled too slowly, the exposure is sufficient, but the bands at those parts of the record where their change of position is most rapid, fuse with each other in the photographic record, and, of course, cannot be interpreted. These difficulties would be lessened had the camera been constructed with an adjustable aperture which could be widened for rapid and narrowed for slow speeds, instead of with a fixed aperture. Even then, however, the margin between the two limits of speed would be small. As constructed the instrument lends itself, when the pulse rate is 70 per minute, to the recording of about one and one-half to three cardiac cycles. For most purposes, both clinical and experimental, however, a record as brief as this is not satisfactory. The film carrier should be constructed to take a record several times this length.

3. *Interpretation of the Photographic Record.* It is the interpretation of the photographic record itself, however, which presents the greatest difficulty. If at any point the movement of the bands has been so rapid as to cause them to blend, or if for any other reason the record is obscured at one point, the relation of the bands to each other on the two sides of this point cannot be determined. In addition to this, the impossibility, in experimental work, of using the machine for fluid transmission of pulse waves instead of for air transmission, is often a serious defect. Still more serious is the fact that a base line cannot be established.

Finally, very minute waves are at times present. These average about 250 to the second, are of very small amplitude, and sometimes can be shown to be artifacts, due to vibrations in the instrument. The plotting of these minute waves is most arduous, yet if the investigator assume the right to plot them or not, as he sees fit, an opportunity for subjective error is at once introduced. This is particularly true in the study of murmurs and heart sounds, and the smaller waves of the pulse. It is, however, the study of these sound waves and smaller waves of the pulse, which is the chief excuse for the use of an instrument of such great sensitiveness as the Crehore micrograph, but in this, unfortunately, it fails. The importance of the study of these smaller waves and of the time relations of the sound waves of the heart to the phases of the cardiac

cycle is suggested by Frank's[3] work with his mirror manometer, as also by Veiel,[4] Müller and Weiss,[5] Weber and Wirth[6] with the same instrument, and by the work of Einthoven and others with the string galvanometer.

In conclusion let us point out that the Crehore micrograph, even if free from technical defects, has no advantages not offered by the mirror manometer of Frank. Moreover, the latter is an exceedingly simple apparatus to operate, is apparently as sensitive to the small waves of the pulse and to sound waves as is the Crehore micrograph, if not more so, gives a photographic record that does not have to be plotted, but can be published directly, and if for any reason the record is defective at one point, this in no way impairs the interpretation of the other parts of the record. Furthermore, a base line is readily established and the instrument lends itself to water transmission of impulses as well as to air transmission.

[3] Zeit. f. Biol., 1904–05, xlvi, 441.
[4] Deut. Arch. f. klin. Med., 1912, cv, 249.
[5] Ibid., 1912, cv, 320.
[6] Ibid., 1912, cv, 562

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia, etc. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, etc. Vol. I, pp. 377; 7 illustrations. Philadelphia and New York: Lea & Febiger, March, 1912.

THE first volume of *Progressive Medicine* for this year has recently appeared. The opening section of 101 pages by Charles H. Frazier is an excellent critical review of the surgery of the head, neck, and thorax. He first takes up the brain and under this heading describes, along with other interesting topics, the hypophysis, cerebral decompression, brain puncture, hydrocephalus, brain tumors, and cranial fractures. After he covers comprehensively the mouth, face, jaw, and neck, he devotes 18 pages to a consideration of the thyroid gland, the parathyroids, and the thymus. Under thoracic surgery Frazier discusses the mammary gland; the heart and pericardium; intratracheal sufflation, over which he is justly enthusiastic; empyema; the surgical treatment of pulmonary tuberculosis, and other phases of the surgery of the lungs and the esophagus.

John Ruhräh has contributed, as usual, an admirable review of the extensive literature on infectious diseases that has appeared during the last year. It is out of the question to attempt to enumerate in detail the wealth of interesting material discussed in this contribution of 144 pages. Among some of the subjects to which particular attention has been paid, may be mentioned Brill's disease, cholera, diphtheria, hookworm disease, malaria, Malta fever, the work of Anderson and Goldberger on experimental measles in the monkey, pellagra, poliomyelitis, scarlet fever, and smallpox. In addition, however, Ruhräh has entered into the always important subjects of tuberculosis and typhoid fever with unusual thoroughness, devoting 35 pages to their consideration.

Diseases of children are covered in 32 pages by Floyd M. Crandall, who emphasizes in particular hemorrhagic diseases of infants, the urine and purulent infections of the urinary tract in infants, indi-

gestion in older children and gastric disorders in infants, and concludes with a discussion of infant foods and artificial feeding.

The last 89 pages of this volume are devoted to a contribution by D. Braden Kyle of 52 pages on rhinology and laryngology and one on otology by Arthur B. Duel. Kyle lays particular stress upon vasomotor disturbances of the nose, common colds, the ocular symptoms and other complications of sinus disease, the tonsils, cancer of the larynx, and the treatment of stuttering. The major portion of Duel's article is taken up with a discussion of syphilis, otosclerosis, diseases of the labyrinth, and the organs of hearing and multiple sclerosis.

A survey of the interesting and carefully compiled information contained in Vol. I makes it evident that during 1912, as heretofore, *Progressive Medicine* must be accorded first rank among current works of reference. G. M. P.

THE SENSIBILITY OF THE ALIMENTARY CANAL. By ARTHUR F. HERTZ, M.A., M.D., F.R.C.P. Pp. 83. London: Henry Frowde and Hodder & Stoughton, 1911.

UNDER this title were delivered the Goulstonian Lectures at the Royal College of Physicians, in March of 1911. The experimental work forming the foundation of this publication was undertaken with the object of interpreting pathological sensations in the alimentary tract, on the basis of disturbance of sensibility of healthy organs. With this object in mind, various divisions of the digestive apparatus have been studiously investigated as to their reaction to tactile, thermal, and chemical stimuli, and on what depend the sensations of fulness and distention, the sensations of emptiness and hunger, and the sensation of pain.

There has been a great deal of experimental work devoted to this study of Dr. Hertz, and we congratulate him on the zeal with which he has attacked the subject, and on the interesting way in which he offers his results to our critical eye. The original lectures have been slightly changed in order to bring the reading matter into a chapteral arrangement. Although the author's trend of thought is easily followed, the impression of facts gathered is reinforced by a very concise summary or *resume* at the close of certain chapters, and at the end of the book by a most contracted list of conclusions.

The chapter on pain has interested the reviewer the most.

Having reviewed for this JOURNAL about a year ago, the book by Mackenzie on *Symptoms*, the writer was interested in noting the divergent view of Hertz from that of Mackenzie on the cause

of visceral pain. The former's credo is tersely expressed in the following words: "I believe that tension is the only cause of true visceral pain," while the latter's theory is based on the production of the viscerosensory reflex. In this chapter, on page 57, appears this sentence: "The contact of free hydrochloric acid with the intact mucous membrane, and with the surface of an ulcer, does not itself cause pain;" while on page 58 appears this: "Consequently an hour or more may pass before there is sufficient free acid to irritate an ulcer near the pylorus." Later: "An ulcer in this (intermediate portion of the stomach) situation, is irritated by acid at an interval after a meal," etc. Several readings of parts of the book calculated to clear up this apparent contradiction were productive of no enlightment of the reviewer's confusion.

The work is interesting, and being mostly original, the opinion regarding it should be conservative until more work has been done along similar lines by other investigators. E. H. G.

TEXT-BOOK OF PATHOLOGY. By FRANCIS DELAFIELD, M.D., LL.D., Emeritus Professor of the Practice of Medicine, College of Physicians and Surgeons, Columbia University, and T. MITCHELL PRUDDEN, M.D., LL.D., Emeritus Professor of Pathology, College of Physicians and Surgeons, Columbia University, New York. Ninth edition. Pp. 1114; 13 full-page plates; 687 illustrations. New York: William Wood & Co., 1911.

THE latest edition of this well-known work has been considerably extended both by additions to the text and by the insertion of over forty new illustrations which are well chosen and add much to the value of the work. Part first, dealing with general pathology, has been rewritten and expanded. The chapter on inflammation is clear and includes complete directions for the experimental demonstration of the phenomena of inflammation. To the chapter on immunity has been added a section on anaphylaxis and one on the technique of the common serological procedures; that of the Wassermann reaction is added to the section on syphilis. The extensive use of the term "alexin" for the now almost universally accepted term "complement" seems unfortunate. Stains for treponema pallidum and for Negri bodies are described. A new chapter on the common malformations, well illustrated, has been introduced. The chapter on tumors has been rewritten. The descriptions of the various tumors is necessarily brief; that of chorionepithelioma, with illustrations, has been added. In outlining the theories of tumor production Ribbert's, in its recently modified form, is emphasized rather more strongly than the others.

A section on tumor transplantation has been added and references cited as recently as 1910.

In part second, dealing with special pathology, the physiological determination of the alkalinity of the blood and the significance of leukocytic ferments are considered. The leukemias and Hodgkin's disease have been rewritten; the latter is particularly complete and well illustrated. The ductless glands receive only brief mention. In discussing fatty degeneration of the liver the authors still hold to the old view now discarded by many pathologists that the fat is formed by a retrograde metamorphosis of the proteid elements of the protoplasm. Mention is made of Opie's production of experimental acute yellow atrophy, and also briefly of the various attempts to produce experimental cirrhosis. The discussion of nephritis has not been altered, but is an exceedingly clear exposition of the subject; the difficulty of correlating the pathological and the clinical types is recognized.

Part third, devoted to autopsy technique and to the preservation and study of tissues, is practically unaltered except for the addition of three illustrations showing the method of opening the heart. This section of the book is brief, but sufficiently detailed to be of value to the student. The references to the literature throughout the book are well chosen and are most valuable. They are selected especially with a view to the bibliographies they contain. They are cited as recently as 1910 (in one instance 1911), on those subjects on which work has been recently done. The index is good and includes an authors' index of all references cited. The authors are to be congratulated upon the marked improvements made in a work already one of the standard text-books on its subject. J. H. A.

LEHRBUCH DER KYSTOSKOPIE UND STEREOKYSTOPHOTOGRAPHISHER ATLAS. By DR. S. JACOBY, Ehemalig. I. Assistenten von Weiland Geh. Mediz.-rat und A. O. PROF. DR. MAX NITZE an der Universität in Berlin. Pp. 247; 48 stereoscopic plates and 121 illustrations in the text. Leipzig: Werner Klinkhardt, 1911.

THE text occupies 247 pages, and its arrangement is similar to that of other standard works on the same subject. The first four chapters contain a description of cystoscopic construction, including the original Nitze instrument and its numerous modifications. Minute instruction is given in cystoscopic technique, the care of instruments, and the various procedures of an examination, with methods of overcoming difficulties that may present themselves. Exclusive of an excellent chapter dealing with the anatomy and physiology of the bladder and urethra, twenty-seven pages are

devoted to the normal bladder as seen through the cystoscope; normal variations, important landmarks, methods of locating the ureteral orifices, etc., are fully and accurately detailed. The author has succeeded admirably in presenting a vivid description of the pictures observed in the various pathological conditions of the bladder, including not only the common but the rare diseases as well. The technique of ureteral catheterization with its diagnostic importance, pyleography, functional kidney diagnosis, and the possibilities of intravesical treatment by means of the cystoscope are given in detail. The concluding chapter deals with a description of the photographic cystoscope, its mechanism and methods of employment. The forty-eight stereoscopic photographs are attractively presented and remarkably clear but the absence of color detracts greatly from their usefulness in conveying to the reader the actual conditions as viewed through the cystoscope. The author has covered the entire field of cystoscopy in a thorough, scientific, and up-to-date manner which places his book among the best on this important specialty. F. E. K.

TEXT-BOOK OF EMBRYOLOGY. By FREDERICK R. BAILEY, A.M., M.D., formerly Adjunct Professor of Histology and Embryology, and ADAM M. MILLER, A.M., Instructor in Anatomy, College of Physicians and Surgeons (Medical Department of Columbia University). Second edition. Pp. 672; 515 illustrations. New York: William Wood & Co., 1911.

THE book represents the outcome of the authors' practical experience in conducting laboratory courses in embryology for medical students, and is, therefore, intended especially for that class of men. The subject is treated in two parts—general development and organogenesis. Under Part I are considered the structure of the cell and cell division; the sex cells, their maturation and fertilization; segmentation of the fertilized ovum; the formation of the germ layers; fetal membranes and the development of the external form of the body. Under Part II is taken up the normal development of the various systems and organs of the body, with a final chapter on teratogenesis. Each chapter is followed by practical suggestions giving the technique for the study of the subjects treated in that chapter, and by the list of references to original papers for further study. In an appendix is given the more general microscopic technique, and the volume ends with an index of thirty-three pages. The book is well printed on heavy paper, with large clear type. The illustrations are numerous, and are reproduced for the most part from other sources, the remainder being from photomicrographs.

The primary object of the authors was to present to the student of medicine the most important facts of development, at the same time emphasizing those features which bear directly on other branches of medicine. Considering the nature of the subject and the time allowed for its study in the medical school curriculum, their purpose has been well achieved. In such a course of instruction it is impossible to present all parts of the subject equally fully. For instance, when one considers the magnitude of the subject of cytology at the present time, it is easily realized how little of this must suffice for the student after he has entered the medical school. Luckily for the present day student he is learning more and more of the fundamental processes of embryology in his premedical days in courses on the frog and the chick, and this allows more time and gives him better preparation for the study of the histogenesis of the mammalian organs. The portion of the volume devoted to the latter subject is particularly interesting in that it shows in the practical suggestions offered the amount of human material which may be utilized in class teaching. Nowadays more physicians are awake to the value of all stages of the human fetus to the teacher of embryology, and in consequence more of this material is saved, preserved in some convenient fluid, such as 10 per cent. formalin, and turned over to a laboratory.

The obvious criticism is that the authors have attempted to cover too much ground, using all classes of the animal kingdom for their illustrations, but until all students have complete courses in comparative embryology before entering medicine this method of teaching must continue.

Such volumes as this show that embryology is no longer an abstract science, to be learned through charts and diagrams, but one which, like normal and pathological histology, may be demonstrated on actual tissues. W. H. F. A.

ANESTHESIA AND ANALGESIA. By J. D. MORTIMER, M.B. (Lond.), F.R.C.S., Eng. Anesthetist of Royal Waterloo Hospital; Throat Hospital of Golden Square; St. Peter's Hospital for Stone; Instructor Medical Graduate College. Pp. 276; 29 illustrations. London: Hodder and Stoughton and Henry Frowde, 1911.

As the author states this work is in the form of a manual for the general practitioner and student and is essentially a practical treatise. In it no attempt has been made to consider the chemical properties, the history, or the theories concerned in the action of the various drugs used. No mention is made of the more modern

methods that are still on trial and have not as yet been definitely proved safe. Nor is anything said of those methods demanding complicated apparatus and which are used almost exclusively by the specialist.

The care of the patient before and after the anesthesia, the duties and the responsibilities of the anesthetist, and the method of administration of the drug are all described in the fullest detail. Each sign and symptom that might arise is described and the remedial measure given.

Each anesthetic is then discussed separately with the method of its administration, its advantages, indications, and contra-indications. The author contends after a large experience that an anesthetist should, in each case, consult with the surgeon and choose that anesthesia which will best suit the individual, both as far as the immediate and the remote complications or sequels are concerned.

An interesting and instructive feature of the book is the chapter on the medicolegal position of the anesthetist. The book is of a handy size, but its binding and paper render it rather difficult to leaf over. In one or two instances the illustrations fall short of what could be desired in a work of this type. E. L. E.

A Practical Guide to the Newer Remedies. By J. M. Fortescue-Brickdale, M.A., M.D., Oxon., Lecturer on Pharmacology in the University of Oxford. Pp., 273. New York: William Wood and Co.

This little book fills a gap in the practitioner's office library that will prove of considerable value. It takes up in detail the relative merits of a large number of preparations, many of which are known under proprietary or trade names and yet which are neither patent medicines nor secret remedies, concerning whose efficacy and reliability the busy doctor may be skeptical. The information given concerning these less well-known drugs if properly studied will serve to augment our armamentarium.

A good feature of the book lies in the clearness with which the various classes of drugs are compared one with the other, and for and against whose usefulness all the clinical and experimental evidence (with numerous references to the original literature) has been adduced; and in addition the author expresses his own views as to which drug or drugs in each group has been proved most worthy of confidence.

The scope of the book, while not exhaustive, is sufficiently large. As the author states in his preface and introduction, his object is merely "to pass in review the newer drugs (mainly the result of

synthetic chemistry) the composition of which is published and whose pharmacology has been more or less accurately ascertained, give some account of the properties and dosage of the principal drugs in each class, and to indicate their relative and collective value as accurately as possible by reference to clinical experience, laboratory experiment, and a study of the literature." This the author has admirably succeeded in doing, and in a very practical manner, eliminating as far as possible a too detailed discussion of the more intricate theories of chemistry. He has wisely excluded the animal group of drugs, as well as a consideration of serum and vaccine preparations. In regard to the arsenical group, it is, perhaps, to be regretted that the book was published too early to admit of a review and discussion of the merits of salvarsan.

Among the several excellent chapters, the one devoted to an impartial discussion of the drugs making up the spinal anesthetic group is especially to be commended. V. L.

HANDBOOK OF MEDICAL TREATMENT. A GUIDE TO THERAPEUTICS FOR STUDENTS AND PRACTITIONERS. WITH AN APPENDIX ON DIET. By JAMES BURNET, M.A., M.R.C.P. (Edin.), etc. New York: William Wood & Co., 1911.

THIS little pocket handbook consists of a brief outline of treatment of all medical and dermatological conditions, of some neurological, and a few surgical conditions. In addition, there is an appendix on diet, including infant food. The advice is logical and clearly given, but necessarily extremely brief. The value of such a book is very questionable. In the title the author says the book is a guide for students and practitioners. A student carefully and conscientiously trained at a good medical school has no use for such a book; while in the practitioner it encourages the employment of superficial and careless methods of dealing with cases to consult for advice a book which disposes of the large subject of therapeutics in such a concise and limited manner.

J. H. M., JR.

FORTPFLANZUNG VERERBUNG RASSENHYGIENE. By PROF. MAX V. GRUBER and PRIV. DOZ. DR. ERNST RÜDIN. Pp. 178; 230 illustrations. Munich: J. F. Lehmanns, 1911.

A CATALOGUE of rest and hygiene presented in Dresden in 1911 at the International Hygiene Congress. T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Rapid Method of Diagnosticating Hypercholesterinemia by Means of Saponin.—L. BOIDIN and CH. FLANDIN (*Compt. rend. Soc. de biol.*, Paris, 1912, lxxii, No. 1, 28) find that cholesterin prevents hemolysis by certain hemolytic agents, notably saponin. Boidin and Flandin have made use of this fact in testing blood serum for an excessive cholesterin content. Saponin, the serum to be tested, and washed corpuscles are mixed in certain stated porportions so that, normally, hemolysis will occur at room temperature immediately; within five minutes, completely, partially, or not at all. Thus in a given case it can be stated whether the cholesterin content of the serum to be studied is higher or markedly higher than normal. Boidin and Flandin have never seen a case of marked cholesterinemia not having this power to prevent hemolysis under such conditions, nor any case in which the antihemolytic power was marked which did not show excessive cholesterinemia. Such sera may appear normal, or be derived from jaundiced or lactating patients. They have found that neither of these conditions are necessarily accompanied by hypercholesterinemia. In conclusion Boidin and Flandin claim that the procedure is simple and rapid. It is not delicate, only emphasizing marked cases, without reference to hypocholesterinemia. But in a suspected case this method makes it possible to tell clinically and at once, if the serum is markedly hypercholesterinated.

A Stain for Spirochetes.—T. SHMAMINE (*Zentralbl. f. Bakt., Parasitenk. u. Infektionskr.*, 1911, lxi, 410) proposes the following technique for the staining of spirochetes. With it he obtains satisfactory stains

of Spirochete pallida, even from cultures. (1) Fixation of the preparation in the flame or, better, in methyl alcohol. (2) Place three or four drops of 1 per cent. potassium hydrate on the smear. (3) Add immediately to this several drops of fuchsin solution ("fuchsin, 15 grams; 96 per cent. alcohol;" dilute one part of this with twenty parts of water) or of concentrated aqueous solution of crystal violet. (4) Allow this mixture to act about three minutes; the stain becomes cloudy and a precipitate appears; finally the fluid becomes decolorized. (5) Wash in water, dry, and mount in balsam. If one desires more intense staining, the specimen may be restained two or three times. With crystal violet better results are secured by substituting 4 or 5 per cent. sodium carbonate solution for the sodium hydrate.

Some Points in the Diagnosis and Treatment of Chronic Duodenal Ulcer.—B. G. A. MOYNIHAN (*Lancet*, 1912, clxxxii, 4610, 9), in the diagnosis of duodenal ulcer, emphasizes the importance of a careful history. It has been stated that the picture of disease thus established does not differ notably from that which has been recognized for generations as hyperchlorhydria. Moynihan believes that this is a term to be used strictly to indicate an excess of active HCl in the stomach contents. It is present in most cases of duodenal ulcer during the active stage of ulceration—hence its importance in this disease as an aid to diagnosis —but is found in other diseases, notably appendicitis and cholelithiasis. The persistent presence of an excess of active HCl in the stomach contents is indicative of an organic rather than a functional disorder. *X*-ray examination after a meal of bismuth, with milk, or bread and milk, in uncomplicated cases of ulcer, affords a most striking spectacle. The activity of the stomach is greatly increased, food beginning to pass into the duodenum at once, and continuing with greater rapidity than normal. By the time the pain begins to appear, the stomach is nearly empty, and most of the bismuth has left the duodenum. In cases of active ulceration, a daily examination of the stools will reveal the frequent if not constant presence of blood. Physical examination is only of the slightest value until obstruction develops. The surgical treatment of chronic duodenal ulcer in the majority of cases is gastro-enterostomy. Since both perforation and hemorrhage have occured many weeks or months after the apparently successful operation, Moynihan considers local treatment essential, best carried out by infolding of the ulcer. Moynihan thinks that diseases of the stomach duodenum, and gall-bladder are secondary, due to a primary infection or toxemia originating in some abdominal organ. In many cases the appendix is diseased, though other sources are possible. Hence routine examination of the abdomen is indicated, as development of jejunal or gastrojejunal ulcer close to the anastomosis may be determined by the continuance of the original source of infection if undiscovered.

A Stain for Diphtheria Bacilli.—MARIE RASKIN (*Deutsch. med. Woch.*, 1911, xxxvii, 2384) has devised a new stain for the demonstration of B. diphtheriæ. The mixture consists of: Glacial acetic acid, 5 c.c.; distilled water, 95 c.c.; alcohol, 95 per cent., 100 c.c.; old saturated aqueous solution of methylene blue, 4 c.c.; Ziehl's carbol-fuchsin, 4 c.c.; This mixture is spread over the preparation in a thin layer and drawn

through the flame. The alcohol ignites and burns in eight to ten seconds. After the stain is allowed to act five to six seconds longer, it is washed off with water, the specimen blotted dry, and examined. The polar granules are stained deep blue, the bodies of the bacilli bright red. Even when diphtheria bacilli are few in number in a mixed culture, they are readily seen. The whole procedure requires only twenty to twenty-five seconds. The stain may be kept indefinitely.

Nitroglycerine Poisoning.—R. Read Pirrie (*Practitioner*, 1912, xii, 259) considers the history of nitroglycerine, its method of manufacture, its pharmacological and physiological action, emphasizing the fact that individual susceptibility in poisoning plays an important role. Among workers with the drug, there is a general opinion that it can be absorbed through the intact skin. Some miners are very cautious in handling explosives, other reckless. All nitroglycerine compounds are liable to become frozen at 40° F., and require a temperature of 50° to soften them. When the weather is cold, some miners have "warming pans" for thawing the explosive; others place it next to the bare skin so soon as they enter the pit, when the body heat softens it and renders it in a condition to be worked by the hands into a shape suitable for use. In imperfect explosion carbonic acid, carbon monoxide, and volatilized nitroglycerine may be given off. Thus workers, by absorption or inhalation may be exposed to poisoning. Pirrie reports 7 cases among explosive workers. They complained of varying acute symptoms, especially headache, vomiting, and jaundice in certain cases. There was one case of optic atrophy, analogous, Pirrie believes, to the enlargement of retinal vessels, with blurring of the disk, found in certain dinitrobenzol workers. There was one death. Autopsy was negative save for dark-colored blood. Pirrie concludes that on account of its volatile character, it is difficult to detect the poison chemically. That workers with nitroglycerin are liable to acute poisoning, the effects of which are neither dangerous to life, nor of long duration. The possibility of change in the rentina and optic nerve may be important. For prophylaxis he advises greater care in handling the explosive, and freer ventilation. For treatment of the acute symptoms, fresh air and oxygen inhalations if necessary.

The Passage of Hemoglobin through the Kidneys.—Warrington Yorke (*Annals of Tropical Medicine and Parasitology*, 1911, v, series 7 M., 401) has found that if an isotonic solution of hemoglobin obtained from rabbits' red blood corpuscles was injected into a vein of a normal rabbit, the urine a few minutes later was tinged with hemoglobin. The injection of large amounts under certain conditions caused suppression. The degree of hemoglobinuria did not reach its maximum for several hours after injection, nor did it parallel the hemoglobinemia. Thus, when several large amounts of hemoglobin were injected at stated intervals, the hemoglobinuria resulting from the last injection was usually much less than that following the first, even though at the end the hemoglobinemia was greater. Microscopic examination of such kidneys showed occlusion of the tubules by casts of varying appearance, according as the tissue examined was obtained from animals which succumbed shortly or later after injection. In the early stages,

the casts were found limited to the cortical tubules, not involving Bowman's capsules. They were slightly granular, appearing to consist of a fairly homogeneous material staining like blood. In the later stages, in addition, casts were found in the larger tubules, were much more granular, and in part crystalline. Yorke believes that such were undoubtedly derived from hemoglobin, though not giving a staining reaction for iron. Comparable lesions are found in kidneys of dogs infected with Piroplasma canis, and in human kidneys from patients with blackwater fever and suppression of urine. On the whole, Yorke concludes that hemoglobin is secreted by the epithelium of the convoluted tubules, and the amount eliminated is dependent on its activity.

Human Infection with Tænia Cucumerina.—J. Lins (*Wien. klin. Woch.*, 1911, xxiv, 1595) reports 6 cases of infection of man with Tænia cucumerina (Dipylidium caninum). This parasite is the commonest tape-worm of dogs; it is not infrequent in cats, but rare in man. Only 60 cases of human infection had been recorded previously. Most of the cases have occurred in children two years of age (36), between two and five years there have been 15 cases, 2 cases between nine and twenty years, and only 6 cases in adults (over twenty years). In only 15 instances was more than one worm found. In one of Lins' cases more than 208 intact parasites were passed following treatment; this is the largest number reported. The patient was a woman, aged thirty-eight years. Four of her children were infected with the same parasite. The remaining patient was a woman, aged twenty-nine years. In all 6 cases multiple infections were found.

The Determination of Individual Dosage in Tuberculin Therapy.—William Charles White and Karl H. Van Norman (*Arch. Int. Med.*, 1912, i, 114) describe again a method by which they determine the sensitiveness of an individual to tuberculin by using on the skin a definite quantity of varying dilutions of tuberculin; then having arrived at the dilution which with a given technique will give a minimal cutaneous reaction around the point of scarification, to determine on this basis the quantity of tuberculin of the same strain, which can be given for therapeutic purposes, intracutaneously to produce a reaction of required degree. As there is no possibility of grading the dosage according to the extent of the disease, by this method it is possible to produce the same grade of reaction in any given number of patients. As patients vary in sensitiveness, and as in a few cases it has been found that increasing doses may be given every two weeks with the same or diminishing local reaction as obtained formerly on the minimal cutaneous reaction basis, the dose should be confirmed every three months by a repeated skin test. White and Van Norman believe that tuberculin should be given in only those cases where the maximum temperature does not exceed 99.6°; to patients who are fairly nourished, and whose general outlook seems favorable. In such by the method described, they find that the patients improve much more than when tuberculin is given with the desire of producing tolerance, the patients feeling better, coughing less, and being better able to stand exercise and strain.

SURGERY

UNDER THE CHARGE OF

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Intracranial Path to the Hypophysis Cerebri through the Anterior Cranial Fossa.—Bogojawlensky (*Zentralbl. f. Chir.*, 1912, xxxix, 209) says that the question of the best approach to the pituitary body is not yet decided. According to the figures of Melchior, in 39 cases operated on, the transnasal path of Scloffer was employed with some modifications. Besides the technical difficulties of the work, at a depth of 8 to 10 cm., without any control of the eyes, it is impossible to do the operation aseptically. At the best only a part of the sella turcica can be removed, while the hyperplastically changed hypophysis with the tumor in it, usually extends beyond the limits of the sella turcica. One would expect that the intracranial path would have attracted more attention from the surgeon, but all reported cases which have been performed by this route, either failed or were not completely successful. Above all the approach through the middle fossa, by elevation of the temporal lobe of the brain, will not succeed, because it becomes indispensable to lift very strongly on the brain so that serious damage is unavoidable. It is also difficult to avoid damage to the sinus cavernosus. The path through the anterior fossa avoids these dangers. Two cases were found in the literature in which the operation was done through the anterior fossa. In the first, that of Arthur, the sella turcica was exposed by a two-sided broad craniotomy and elevation of the frontal portion of brain on both sides. Death occurred some hours after the operation. In the second case, that of F. Krause, the intracranial approach was from the right frontal region. Although this patient recovered, the operation which was performed for a sarcoma of the hypophysis accompanied by a bilateral optic atrophy, was followed by a paralysis of the left facial nerve and the left extremities. Bogojawlensky reports the following case: A man, aged thirty-five years, began to complain two years before of a severe headache which was soon continuous and so severe that he became bed-ridden, and for one and one-half years could not sit up. The signs of acromegaly were present. The operation was performed in two stages. In the first an osteoplastic flap, 9 cm. high and as wide, was lifted, its medial border being 2½ cm., from the median line and the lower border 2½ cm. from the upper border of the orbit. One to 1½ cm. of the bony margins of the opening in the skull was removed by

forceps, and with this the operation ended. The second stage of the operation was carried out six weeks later. After elevating the osetoplastic flap, the dura was opened by a H-shaped incision and the flaps turned upward and downward. The head of the patient was then brought over the edge of the table and the right frontal lobe of the brain was separated from the orbital roof, slowly and carefully, first with the finger and then with the Krause brain elevator. This gave a cleft, 5 cm. broad anteriorly, more narrow posteriorly. At a depth of about 7½ to 8 cm., the right optic nerve was visible. A copious escape of cerebrospinal fluid prevented further examination. Raising the head end of the table about 30 degrees stopped this. Just in front of the optic commissure could be seen a dark red tumor which was tongue-shaped. It was removed with a curette which went to the bottom of the sella turcica without difficulty. The bleeding was slight. The dural flaps were sutured, the osteoplastic flap placed in position and the skin sutured. The postoperative course was without disturbance and the eyes were not affected. Three weeks later the symptoms of acromegaly began to disappear. Bogojawlensky considers that the intracranial route through the anterior fossa is not only the best, but the only method by which one can be compleetly aseptic and remove everything from the sella turcica under the control of the eyes, without injuring the brain or the optic nerves. It is necessary to employ artificial light, best in the form of an electric lamp with a reflector on the brow. The best position of the patient is obtained by elevating the end of the table to an angle of 30 degrees, with the head strongly retroflexed.

Nerve Anesthesia in Kidney Operations and Thoracoplasty and in Operations on the Trunk in General.—KAPPIS (*Zentralbl. f. Chir.*, 1912, xxxix, 249) says that novocain-suprarenalin gives us a relatively safe and strong local anesthesia. It is an important advance, particularly when peripheral nerve trunks are injected. It has been employed in operations on the trigeminus region and the extremities. Nephrotomy, amputation of the breast, and thoracoplasty have been done with it. Kappis has used it for a pyelotomy, a nephrolithotomy, and a nephrectomy. The method is as follows: In order to inject the intervertebral nerve, the needle is introduced about 3½ cm. from the midline on a level with the lower border of a rib. The rib in this position is not palpable, but its position can be determined in the following manner. Even in stout individuals somewhere in the back, one of the lower ribs will almost always be palpable. The lower edge projects toward the median line. The needle is to be introduced at a point where the lower edge of the rib is 3½ cm. from the median line. The rib is reached at a depth of about 4 or 5 cm., about in the angle between the transverse process and the rib, which can occasionally be distinctly felt. Keeping as much as possible in this angle at the lower border of the rib, the needle is pushed forward and somewhat medially, and the fluid divided between the level of the rib and 1½ cm. deeper. When the injection has been made under one rib, the other points of injection are easily selected, since one simply keeps in the line 3½ cm. from the median line and goes about 3 cm. upward or downward, seeking in a similar manner the lower edge of the rib and making the

injection. The transverse process of the lumbar vertebræ must always answer for the ribs, but they are further apart than the ribs. Ten cubic centimeters of a 1.5 per cent. novocain-suprarenalin solution is injected. The operation should begin in about a quarter of an hour after the injection. In his first two kidney operations, Kappis injected from the ninth dorsal to the second lumbar vertebra on the affected side. Since the stripping off of the peritoneum was not completely painless, in the next operation, he injected also the seventh and eighth dorsal, but without a better result. With a proper injection, the skin, soft tissues, and kidneys with a large portion of the ureter, will be completely painless, but not so with the stripping of the peritoneum. For this reason he has on one occasion given 15 drops and on another occasion 30 drops of ether. The method is an important advance in kidney operations, especially when the kidney not operated on is diseased. It permits the avoidance of a psotoperative nephritis from the narcosis in the remaining kidney after a nephrectomy.

The Technique of Local Anesthesia in Thoracoplasty.—SCHUMACHER (*Zentralbl. f. Chir.*, 1912, xxxix, 252) says that Sauerbruch employed the following method in 35 cases of extensive rib resections: Small doses of morphine or of pantopton were given one hour before the operation. A 0.5 per cent. novocain solution with the addition of suprarenalin was employed, the solution being made freshly for each operation. According to the extent of the operation, from 10 to 200 c.c. were necessary. The line of the intended incision was first injected subcutaneously. From this anesthetic line the deeper tissues, chiefly the nerves, were injected. The needle was directed from below and inward, upward, and outward against the rib lying over the point of injection in the region of the angle of the rib. When the needle scraped the bone, 1 to 2 c.c. were injected. Then feeling for the lower border of the rib, 5 to 8 c.c. were deposited. At the costal angle the intercostal nerve passes from the middle of the intercostal space upward to the lower border of the rib above. The intercostal veins are already in the groove under the rib above. The injection is made for each rib to be resected. The first intercostal nerve under the first rib is injected successfully in thin patients, but less so in stout patients. For the axillary incision a large injection needle is passed as far as possible posteriorly along the convex border of the rib with continuous injection. In 20 out of the 35 operations, in which 4 to 8 ribs were resected, no chloroform was necessary. In the others a few drops were necessary to induce a partial, light narcosis. No accidents, such as penetration of large vessels, the pleura or lungs, were observed.

Parathyroids and Their Surgical Relation to Goitre.—MAYO and MCGRATH (*Annals of Surgery*, lv, 185) say that numerous hypotheses, erroneous deductions, and illogical conclusions have been drawn in connection with the action of the parathyroids, but that there no longer seems to be substantial grounds for doubting the etiological relationship between them and one disease, namely, tetany. Experimental tetany has been produced in animals by the removal of parathyroid tissue, and experimental tetany may be reckoned, in a certain sense, tetany following operation upon the human thyroid gland.

Spontaneous tetany is caused by an hypoplasia with resultant insufficiency of the parathyroids. Pathological examinations seem to have proved that hemorrhages into the parathyroids have a positive significance in the causation of tetany, especially in childhood, and that these hemorrhages produce their effect by injuring the parathyroidal tissue, inhibiting its development and consequently decreasing its functional power. According to MacCallum and Ovegtlin all violent symptoms produced by parathyroidectomy—muscular twitching and rigidity, tachypnea, fibrillary tremors, increased rapidity of the heart beat, etc.—may be almost instantly cured by the intravenous injection of a solution of a calcium salt. The acetate or lactate in a 5 per cent. solution is usually employed. The condition of relief following the administration of these various salts lasts for perhaps twenty-four hours, when tetany may reappear. Analysis of the blood taken from a dog during tetany shows a calcium content which is only about half that of the normal dog on the same diet. Insufficiency of the parathyroids seems to be necessary for the production of tetany. Gastrointestinal disease may be a contributing factor by causing a hypofunction of the parathyroids, which is the most frequent form of tetany, especially in children. Remembering the variable size, location, and appearance of the parathyroids, the surgeon should preserve all, especially gland-like, masses about the capsule in cases of operation on the thyroid gland. If such a mass be accidentally removed in the course of operation, it should at once be implanted beneath some part of the remaining capsule. According to Vincent and Jolly, the parathyroids left behind after thyroidectomy can, under conditions, develop in the direction of thyroid tissue, and a functional replacement also can take place. The ideal treatment of tetany would be to compensate for the glandular deficiency by transplanting parathyroids from other individuals, feeding with animal glands, the use of serum or the extract of parathyroid tissue. Unfortunately, none of these procedures has given dependable results. No reliable treatment is at present known.

THERAPEUTICS

UNDER THE CHARGE OF

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Transfusion of Blood for Typhoid Hemorrhage.—Booth (*Yale Med. Jour.*, 1912, xviii, 214) reports a severe case of typhoid that was complicated by hemorrhages. The use of the ordinary therapeutic procedures such as hypodermoclysis, injections of rabbit and human serum, and the administration of calcium lactate apparently had no marked benefit. The condition of the patient was so bad that transfusion of blood was done as a last resort. The effect of this was remark-

able, the temperature that was subnormal, rose to normal, and the pulse rate dropped to the same level that preceded the hemorrhage. The transfusion had no effect on the course of the typhoid as the temperature recurred and the patient went through the ordinary course of the disease from the stage before the hemorrhage occurred. Booth wonders if the transfusion of blood from a donor who had recovered from typhoid would have any beneficial effect upon the course of the disease.

The Treatment of Spirillum Affections of the Mouth with Local Applications of Salvarsan.—ZILZ (*Münch. med. Woch.*, 1912, lix, 20) has had good results with the use of local applications of salvarsan to various non-specific ulcerative conditions of the mouth and in various inflammatory conditions of the gums. He also mentions Vincent's angina as among the conditions that are most favorably influenced by this local treatment with salvarsan. The lesions are thoroughly cleansed with warm physiological salt solution, and salvarsan is applied directly in a 10 per cent. aqueous or glycerin solution, or in an oily suspension. The solutions should be made up fresh, but suspensions in paraffin keep for several days. Zilz says that sluggish ulcers clear up rapidly, and show a tendency to heal. Various forms of spirochetæ that occur in great numbers in many mouth inflammations disappear rapidly under the influence of this local treatment.

Therapeutic Injection of Serum or Defibrinated Blood for Hemorrhage or Anemia.—JOHN (*Münch. med. Woch.*, 1912, lix, 186) reports 6 patients with severe intestinal hemorrhages in the course of typhoid fever apparently cured by injections of defibrinated blood. He draws from 30 to 50 c.c. of blood from a vein in the arm of a healthy person into a glass vessel containing some glass beads. The blood is then defibrinated by vigoriously shaking the vessel. He injects the defibrinated blood into the gluteal muscles or subcutaneously. This injection is repeated two or three times at two or three day intervals. John has had equally good results with this method in a case of pernicious anemia. The hemoglobin percentage in this patient had dropped from 38 to 19, and the red cells from 2,200,000 to 600,000 during a month of the usual methods of treatment. This patient received two injections of serum alone. Six weeks after the injections the hemoglobin had risen to 62 per cent., and red cells to 3,500,000. Esch has also reported similar results in 2 cases of pernicious anemia, and he attributes the benefit from the defibrinated blood or serum to a stimulating action of the alien blood on the red bone marrow. John says that when it is difficult to obtain fresh blood, fresh horse serum should be tried in any severe hemorrhage that cannot be controlled by the usual measures.

Codeonal, a New Hypnotic and Sedative.—GAUPP (*Berl. klin. Woch.*, 1912, xlix, 306) says that codeonal appears to be a very efficient hypnotic in certain conditions that usually require morphine. Codeonal is a combination of codine and veronal. It is especially applicable in cases where insomnia is due to pain or when there is distressing dyspnea or cough. It is an efficient hypnotic when it is given to replace

a drug to which a patient has become accustomed. Gaupp says there are no untoward symptoms from its use. It is often of advantage to combine codeonal with sodium-veronal, giving the codeonal in a dose of 0.04 grain and the sodium-veronal in a dose of 0.3 grain.

Streptococcus Vaccines in Scarlet Fever Prophylaxis.—WATTERS (*Jour. Amer. Med. Assoc.*, 1912, lviii, 546) was led to try the effect of streptococcus vaccines as a prophylactic measure against scarlet fever by the work of Grabeitschrewsky. His method as described consists in the administration of broth cultures of streptococci in doses of about 0.5 c.c., previously killed by heat and phenol. The injections are given about once a week. After using the vaccine in 700 cases he concluded that it had a decided value from a prophylactic standpoint. A number of other Russians arrived at similar conclusions with a trial of this same method. Watters administered a polyvalent vaccine made of a number of different strains of streptococci that were isolated from the throats of scarlet fever patients. The vaccines were given to nurses who were exposed to the disease in scarlet fever wards. The initial dose given was 50,000,000 of the polyvalent streptococci vaccine about two or three weeks before the nurse went on duty in the wards. This injection was usually followed by some local reaction, soreness of the arm, and occasionally by some general manifestations such as headache or malaise. A second dose of 100,000,000 was given a week later, and a third dose of 200,000,000 at the interval of another week. In comparing the effects observed he states that but one very light case of scarlet fever has occurred among the nurses who have received vaccine treatment, while in a considerably smaller group, under identical conditions, 5 developed severe cases of scarlet fever. Watters does not attempt to draw any conclusions from the small number of cases but he thinks that the results of the vaccine treatment were very suggestive and that the method is worthy of further trial.

The Serum Treatment of Hemorrhage and Blood Dyscrasias.—LESCOHIER (*New York Med. Jour.*, 1912, xcv, 223) reviews at length the serum treatment of hemophilia and other allied diseases, and draws conclusions as follows: The coagulation time of the blood in hemophilic subjects is greatly shortened by the injection of fresh serum of any species. The sera of the ox and dog should be avoided because they are more apt to produce toxic symptoms. The local application of fresh serum to wounds in patients with delayed coagulation tends to act as a hemostatic. Regular antitoxic sera are less satisfactory than freshly drawn material. The action of serum in accelerating blood coagulation is apparently due to a substitution of active thrombin.

Therapeutic Results of Radium Emanations.—BENCZUR (*Berl. klin. Woch.*, 1912, xlix, 108) reports 60 cases of various diseases treated by radium emanations given by mouth and also by subcutaneous injections. The treatment was given during a period of from four to eight weeks. The amount given daily was about 1000 Mache units. In 12 cases of tabes the lightning pains were very favorably influenced. The treatment had no effect in 2 cases of tabes who were addicted to the

morphine habit. A number of different forms of neuralgia were much benefited by the radium treatment. Four cases of sciatica were cured; 2 other cases, on the other hand, were not at all influenced by the treatment. The majority of the cases of chronic polyarthritis were also much benefited. The radium emanations seemed to have little or no effect in cases of chronic muscular rheumatism and lumbago. Benczur believes that the curative effect of radium emanations is largely dependent upon the vascular dilatation produced by the remedy, and he has observed a tendency to hemorrhage in a number of the patients during the treatment.

PEDIATRICS

UNDER THE CHARGE OF

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Diphtheria of the Esophagus.—J. D. ROLLESTON (*Brit. Jour. Child. Dis.*, 1912, ix, 12) reports a case of diphtheria of the esophagus in a boy, aged two years. The child when admitted to the hospital was practically moribund from diphtheria involving the nasopharynx and pharynx, with diphtheretic excoriations on one ear and the left malleolus. He had received no antitoxin. Cultures of all the lesions showed the Klebs-Loeffler bacillus. There was marked loss of substance in the left side of the pharynx. The autopsy showed a normal trachea. The esophagus in its upper third was apparently normal, the middle third showed some injection of the mucosa, while in the lower third were two longitudinal areas of necrosis, coalescing below, and about 3.5 cm. in length. The muscular wall was exposed in one area. The diphtheretic membrane had disappeared, but direct smears and cultures showed numerous diphtheria bacilli. This condition is rare, and usually is associated with multiple lesions elsewhere. During life the subsequent development of an esophageal stricture is the only means of making a diagnosis. Mallory reports 251 necropsies in diphtheria in which the above condition was found in 12 cases. In other cases the condition may be due to scarlet fever, since Oppikofer found 15 cases in 128 scarlet fever necropsies. Among cases reported in literature the end results have been perforation of the esophagus, expulsion of the cast with recovery, and the development, subsequently, of an esophageal stricture. In the last named result all cases recovered by gradual dilatation of the stricture by bougies. The frequent use of bougies in strictures from other causes may predispose to diphtheria of the esophagus.

Acute Benzine-poisoning in an Infant.—ADOLPH FRIEDIGER (*Münch. med. Woch.*, 1912, lix, 252) found in literature the reports of 14 cases of poisoning in infants by swallowing benzine. Eight of these died and the others recovered after symptoms of more or less severe intoxication. In but one case was a child reported as poisoned by

inhaling benzine fumes. According to the observations of various authors, benzine exerts a particular toxic effect on the central nervous system, the gastro-intestinal tract, the lungs, and the pleura. Convulsions and vomiting are common and the latter occurs in the inhalation cases also, though less severely. The vomiting of blood and mucus and a diarrhea of the same character occur in cases in which the benzine has been swallowed. The heart action is rapid and irregular and disturbed breathing is common. The temperature rises, in some reported cases to 40.2° C. Loss of consciousness often occurs with great suddenness. Friediger reports his own case of an infant, aged six weeks, which he had been treating for furunculosis complicating an eczema, anemia, and general malnutrition. The infant was much improved and adhesive plaster was being used as a dressing for furuncular areas on the trunk. On one day benzine was employed to loosen the adhesive and cleanse the skin, a fresh adhesive dressing being placed on the various areas. Almost immediately afterward the child became restless, began to vomit, and to have convulsive movements. Within twenty-four hours the child presented absolute pallor, emaciation, expulsive vomiting, convulsions, dyspnea, retracted abdomen, fever, and rapid pulse. It became practically moribund. Immersion in wheat-bran baths and cool sponges improved the condition, and in twenty-four hours the child's condition was good and the toxic symptoms had disappeared. The points of interest in this case are the age of the child (six weeks), and the poisoning by inhalation of fumes from the local application of benzine. Absorption through the skin was possibly a further factor. The case further indicates the danger of the local use of benzine on very young infants with very weak constitutions.

The Eucalyptus Treatment in Scarlet Fever.—E. KOERBER (*Münch. Med. Woch.*, 1912, lix, 581), reports the results obtained by Dr. Rumpel in Eppendorf in testing the eucalyptus treatment in scarlet fever as practised by Milne in England. Milne applies twice daily for the first four days the pure eucalyptus oil to the entire body surface and repeats this once daily for the following six days. He also applies a 10 per cent. solution of carbolic acid in oil to the tonsils every two hours for the first two days. His patients are not isolated and he claims no contagion to unprotected children resulting, either during or after the disease. In an epidemic in Eppendorf the cases were divided as to treatment for the sake of comparison. There were 274 cases treated in the usual manner and 151 with the method of Milne: Infection was transmitted by cases returned to their homes as cured in the following proportions. In 86 cases not treated with eucalyptus oil it occurred 3 times, or 3.5 per cent. In 73 cases treated with eucalyptus oil it occurred 4 times, or 5.5 per cent. Those cases only were reported where the family could be under close observation constantly, thus ruling out infection from other sources. The mortality was only 0.56 per cent. less in the encalyptus series. It was noteworthy, however, that the complications of endocarditis, nephritis, glandular suppuration, and otitis were 50 per cent. less frequent in the eucalyptus series than under the ordinary treatment. The joint complications however, were more frequent. A shortening of the course of the disease with the eucalyptus treatment was not observed. The period of infectivity

was not shortened, one of the return cases infecting the family three months after the primary onset. Therefore the authors are not convinced of Milne's claims from the above experiences in Eppendorf.

Purpura in Infective Diarrhea.—H. D. ROLLESTON and J. B. MOLONY (*Brit. Jour. Child. Dis.*, 1912, ix, 1) analyzed 100 cases of infective diarrhea in infants to determine the frequency of symptomatic purpura in this disease. Of the 100 cases, averaging infants from seven to eighth months and of both sexes, 67 proved fatal. Of the 67, 16.4 per cent. showed purpura. None of the purpuric cases showed edema. The abdomen and thorax is the frequent site of the purpuric eruption, though the arms and legs are occasionally involved. The hemorrhages are usually small, but may be so closely set as to make the abdomen appear uniformly purple from a distance. The purpura was usually a late symptom and appeared about the thirty-fourth day, a week before death. Occasionally the hemorrhages came out in crops. Transfusion and the administration of horse or other serum seemed to have no influence in causing purpura. In one case only was there evidence of infantile scurvy. No close relation is suggested between purpura and the edema sometimes seen in infective diarrhea. The prognosis appears extremely grave, as all the cases mentioned above died. Voelcker, however, says it is by no means a necessarily fatal sign. To conclude, symptomatic purpura in infective diarrhea mainly occurs on the abdomen and chest of infants under one year of age. It is usually a terminal phenomenon in prolonged cases, and the prognosis is extremely grave.

Drunkards' Children among the Weaklings at School.—EUGEN SCHLESINGER (*Münch. Med. Woch.*, 1912, lix, 649), reporting his observations on weak and backward school children, states that the two important factors in the inherited low resistance and organic weakness of many children are, first, a neuro-psychopathic constitution of the parents, and second, alcoholism in the parent. Next in importance and frequency is syphilis. Out of 200 weaklings studied, Schlesinger found 30 per cent. who were the children of drunkards. A percentage of 40 to 60 was found in severe intellectual weakness, in imbecility, and idiocy. The low vitality found in drunkards' children is traced back to the female parent. Sullivan and Arrivé state that 55 per cent. of the children of alcoholic mothers die either at birth or within two years. The extent of the degeneration in the children can be gauged by their constitution. Only 33 per cent. of them were in good constitution, 57 per cent. only fair, and 9 per cent. very poor. These unfortunate children show nutritional disturbances, catarrh of the respiratory tract, and especially lowered immunity to infections from their first year of life. The most intense and destructive effects of this heredity are seen in the central nervous system, especially the motor side, resulting in convulsive attacks, tic, and epilepsy. While defective intelligence was probably not more marked in the drunkards' children than in other defectives, the psychic, ethical, and moral defectiveness was well marked and combined with an unstable, mercurial temperament. A tendency toward alcoholism is often observed in the offspring of alcoholics. The future of such children is unpromising and an early severing of home associations and strict disciplinary schooling is imperative.

OBSTETRICS

UNDER THE CHARGE OF

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Tuberculosis and Pregnancy.—CRISOTOFOLETTI and THALER (*Monats. f Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 5) give the results of their clinical obsrevations in experimental researches on this subject, from Schauta's clinic in Vienna. As regards the frequency of this complication, it is usually stated that pregnancy exercises a practically fatal influence over tuberculosis in from 20 to 50 per cent. of all tuberculous women who conceive. In view of this fact it becomes of the greatest importance to ascertain what is the duty of the obstetrician regarding the interruption of pregnancy. The fact that pulmonary tuberculosis usually begins in the apices explains the fatal influence of pregnancy, as pregnancy lessens the expansion of the lungs and interferes considerably with pulmonary circulation. Another factor of importance is the changes in the connective tissue of the lungs and epithelia and the respiratory tract which usually accompany gestation. To disturb the metabolism of pregnancy further complicates the situation. In some cases the inspiration of infectious secretion during actual labor to healthy portions of the lung aids in spreading the tuberculous process. From this and other causes it follows that tuberculosis is most increased during the second half of pregnancy. When the blood serum of the pregnant patient and that of the non-pregnant is studied, one is unable to demonstrate any essential difference which should materially influence the tubercle bacillus. It is thought by Hofbauer and Stern that an indirect relation exists between the lipoid condition of pregnancy and the spread of tuberculosis. It is also thought that the pregnant condition in this regard tends to increase the virulence of the tubercle bacillus. There are many conditions peculiar to pregnancy in disturbed metabolism which are favorable for the development of infection. When the question of the interruption of pregnancy is considered, it is thought that in advanced gestation the interruption of pregnancy exposes the patient to greater danger than spontaneous labor and the puerperal period. The removal of the pregnant uterus in the second half of gestation would certainly inflict as great trauma as parturition. The prolonged interference necessary for the induction of labor is also unfavorable. As regards sterilization of tuberculous patients during the second half of pregnancy by the removal of a portion of the Fallopian tubes, this operation is much more favorably undertaken in the first three or four months of gestation. Where pregnancy has been interrupted the patient is exposed to great danger should conception speedily recur. The use of the *x*-rays to produce sterility has not been proved of definite value. It is believed that where pregnancy is to be interrupted the contents of the uterus should be removed, fol-

lowed by operation upon the tubes by vaginal incision. In 41 cases this procedure resulted successfully. The effort is made to operate practically outside the peritoneum by traction upon the uterus and round ligaments with tenaculum forceps, making it feasible to secure the insertion of the tube in the peritoneal wound. The excision of a considerable part of the tube at the isthmus is efficient. This method, however, should be limited to the early months, and should not be performed later than the third month. After this time general narcosis is necessary, and pure chloroform is given where there is much expectoration, or lumbar anesthesia is selected. By experiment upon animals, it is found that guinea-pigs from which the ovaries have been removed show a lessened tendency to the spread of tuberculosis, although such animals often show less resistance to a primary infection.

Ectopic Pregnancy Twice in the Same Patient in Six Months, Necessitating Two Laparotomies.—OLIVER (*Brit. Med. Jour.*, December 23, 1911) reports the case of a patient in her second pregnancy, seven weeks advanced, suddenly seized with severe pain in the lower abdomen, and a hemorrhagic discharge. Although operation was not performed for nearly a month there was a continuous vaginal hemorrhage, and three separate attacks of pain. On examination the uterus was not enlarged, and a small swelling was found in the lower portion of the abdomen, with great tenderness. At operation the omentum and intestine was adherent to a swelling in the left posterior segment of the pelvis. On separating the adhesions dark blood immediately escaped. The left tube and ovary were removed, the tube containing an embryo of six or seven weeks, with a quantity of blood clot. Menstruation returned two months after operation, and was normal. The next period was missed, followed by slight pain in the abdomen, with vaginal hemorrhage. A month later, on palpating the abdomen there was slight tenderness in the right iliac region, the body of the uterus was not enlarged, and behind the uterus to the right was a small dense, movable swelling, slightly tender. At the second operation the small intestine was extensively adherent to the tumor. The hematoma burst as soon as grasped, and the right tube and ovary were removed. The tube contained an embryo about three-eighths of an inch in length. The patient made an uninterrupted recovery.

Changes in the Quantity of Blood in Pregnancy, Labor, and the Puerperal Period.—FRIES (*Zeits. f. Geburts. u. Gynäk.*, 1911 Band lxix, Heft 2,) has conducted a series of experiments to ascertain what variation, if any, takes place in the quantity of blood in pregnancy, parturition, and the puerperal period. He finds that during pregnancy a slight diminution in the relative quantity of blood, as compared to the body weight, takes place. During labor and the puerperal period this is succeeded by a gradual rise to the normal, while the quantity of blood, in proportion to the body weight, is often considerably increased in contrast to a loss of body weight at this time. These facts are interesting in connection with pathological conditions occurring during pregnancy, such as eclampsia, heart lesions, unusual plethora, or anemia.

GYNECOLOGY

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Artificial Occlusion of the Ureter.—It occasionally becomes necessary during operations for malignant conditions of the lower abdomen, to resect a considerable portion of a ureter that reimplantation into the bladder, or direct suture of the cut ends, is out of the question. Among the various ways of dealing with this situation one of the simplest, at least theoretically, is that of throwing the corresponding kidney out of function by occluding the ureter. That this is not always so simple as it seems, however, was pointed out by Stoeckel in a paper recently reviewed in these pages. At Stoeckel's suggestion, therefore, a series of experiments to determine the best method of accomplishing this result have been carried out on animals by KAWASOYE (*Zeit. f. gyn. Urologie*, 1912, iii, 113). He tested the occluding effect on the severed ureter of four methods of procedure: (1) Simple ligation, (2) the formation of a two-limbed, U-shaped kink, the two limbs being tightly tied together, (3) the formation of a three-limbed, Z-shaped kink, the three parallel limbs being sewed together with catgut, and a simple ligature in addition being thrown around the ureter distal to the kink, (4) the formation of a true knot in the ureter, distal to which a simple ligature was placed. Only the last of these methods has proved trustworthy in causing complete occlusion of the ureter. This is due to the fact that in all ligation methods in which stasis of the urine or dilatation of the ureter occurs immediately above the ligature the latter in every case breaks into the lumen, with the formation of a fistula or abscess, even though great care be taken not to injure the wall in applying the ligature. The true occlusion of the lumen, due to organization, which occurs below the ligature is hence of no avail. A *sine qua non*, therefore, for the production of a satisfactory occlusion is the introduction of a kink *between* the ligature and the portion of the ureter which is to undergo dilatation, and this kink must be produced without the use of ligatures or sutures, conditions which are best fulfilled by tying the ureter in a knot. This allows at most so little urine to trickle through that the ligature placed about the ureter below it is subjected to no pressure, and is able, without breaking through, to produce complete obliteration of the lumen by fibrous organization.

Bacteriological Examinations during Gynecological Operations.—With a view to ascertaining the bacteriologic conditions that may exist in the abdominal wound and in the peritoneum during various classes of operations, and especially in order to determine the importance of so-called "endogenous infection," BAUEREISEN (*Zentralbl. f. Gyn.*, 1912, xxxvi, 386) has been for a long time taking systematic cultures during the course of his operations. This is done by means of small, sterile

swabs, which are immediately placed in bouillon, from which aërobic and anaërobic blood-agar plates are made after twenty-four hours. He reports the results obtained in 340 cases; 254 of these were laparotomies, the remainder various procedures, largely extensive vaginal operations. The peritoneum was found sterile in but 80 of the 254 laparotomies, and in but 11 of 42 vaginal hysterectomies. Infection was found present especially frequently in carcinoma cases, the peritoneum being found free of organisms in only 2 out of 43 abdominal operations for this condition, and in none of 3 vaginal ones. The abdominal wound was found sterile throughout the operation in only 30 cases. Bauereisen believes that while "endogenous organisms" exist very often, they play an important role only in carcinoma cases, in which they can remain virulent, owing to the favorable cultural conditions furnished by the large area of tissue of poor resistance left after the radical operation. He believes that the vaginal secretion should always be considered unsterile and dangerous, and that the vagina should therefore be thoroughly disinfected before every gynecological operation. To him, "autoinfection," surgically considered, means merely the artificial infection of the wound, during operation, by endogenous organisms. He has attempted to find some means of establishing a more or less certain prognosis from the bacteriologic findings during operation, but has been unable to do this, since bacteriologic methods do not as yet enable us to distinguish with certainty between virulent and avirulent organisms, nor to measure in any accurate way the important factor of the resistance of the patient. Bauereisen says that by carefully protecting the edges of the abdomianl wound from every possible contact with the contents of the peritoneal cavity, he has been able to produce a marked reduction in the number of infected wounds, this being especially striking in the carinoma cases. Using a sheet of "Billroth-battist" over the abdomen, which is incised at the operation, and is fastened exactly to the wound surfaces by means of the Stoeckel speculum, he has attained in many instances healing *per primam*, notwithstanding the presence of large numbers of microörganisms in the peritoneum. This, he thinks, is so far the most tangible result of his bacteriologic studies, but he also considers such examinations of great value in enabling an operator from time to time to control his entire aseptic technique.

Surgical Treatment of Polycystic Kidney.—Rovsing (*Amer. Jour. Urology*, 1912, viii, 120) reports a series of 3 cases of this disease in which distressing symptoms were greatly relieved, and the life of the patients apparently prolonged, by exposing the more affected kidney and performing multiple punctures of the cysts. Since the condition is practically always bilateral, nephrectomy is, except in rare instances, positively contraindicated, and yet severe pain, oliguria, and other severe symptoms demand intervention. Rovsing's first case was a male, aged forty-one years, who suffered from severe pains in the left kidney region. The organ was found at operation to be 18 cm. in length, nodular, and multicystic. First the superficial and then the deeper cysts were punctured, no hemorrhage resulting. The kidney, thus reduced to half its former size, was replaced, and a gauze drain soaked in silver nitrate introduced into the wound. For three days there was a slight discharge of urinous fluid into the dressing, but this then ceased; there was no permanent fistula formed, and no extension of the kidney

tumor into the perirenal tissue, both of which eventualities had been feared by Rovsing. The patient was entirely relieved of his pain; his urinary output increased from 1500 c.c. before operation to 2000 c.c. after, and he lived three years, finally dying of uremia following a fever. The second and third cases were women, aged about fifty years, who presented similar symptoms, and were treated in the same manner. In the second case albuminuria was present; after operation the albumen was greatly reduced in amount, the urinary output tripled, and the urea excretion doubled. In the third case the urinary output was increased from 440 c.c. before operation to 1250 c.c. after, and the urea excretion was increased eight fold. In both these cases also the pain entirely disappeared. Rovsing explains these phenomena on the ground that in polycystic kidney disease normal renal tissue is present between the cysts, but its action is inhibited by pressure; when this is relieved, normal kidney function is reëstablished, and the general condition of the patient thus improved. He does not claim that the procedure is more than palliative, but believes that it is of value in relieving symptoms and prolonging life. In an article upon the same subject, BALFOUR (*Journal-Lancet*, 1912, xxxii, 170) reports 2 cases from the Mayo clinic which were treated along similar lines. The first case was that of a woman, aged forty-seven years, in whom at operation one kidney was found to contain a cyst the size of the adult head; the remainder of that kidney, and the kidney of the opposite side, were filled with cysts of all sizes up to that of an orange. In this instance the large cyst only was opened, emptied of about a quart of fluid, and then partially enucleated. The remainder of the sac was sutured to a stab wound, and drainage introduced, but no fluid came away. The patient made an uneventful recovery. In the second case there was a preceding history of injury, which had led to the diagnosis of rupture of the kidney. At operation, however, a cystic kidney was found, the cysts varying in size from that of a pea up to a grape-fruit. The larger cysts were opened and emptied of their contents, reducing the bulk of the organ by three-fourths. Three cigarette drains were introduced, but no fluid whatever came away. This patient likewise recovered.

A New Operation for Retroversio Uteri.—An addition to the long list of operations that have been devised for the treatment of this condition has been made by HEUSNER (*Zentralbl. f. Gyn.*, 1912, xxxvi, 393). He considers the broad ligaments, and especially the cardinal ligaments, which pass through their bases, the most important factors in holding the uterus in its normal anteverted position. Acting on this supposition, he has devised an operation which consists merely in folding together the two broad ligaments behind the uterus, a process which can easily be carried out when they are relaxed. Where the two ligaments meet in the median line posteriorly they are stitched together by a few mattress sutures, thus supporting the uterus in a broad sling, and having much the same relation to that organ that the wings of a bird, folded over its back, have to its body. The ureters remain a finger's breadth below the lowest mattress suture, and are not in any danger; neither are the uterine arteries. Heusner has worked out the operation on the cadaver, and has done it on two patients, with apparently satisfactory results, although sufficient time has not elapsed to judge of the lasting effect.

OTOLOGY

UNDER THE CHARGE OF
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The Fistula Symptom.—G. ALAGNA (*La pratica oto-rino-laringoiatrica*, No. 6, 1911), recognizing the horizontal semicircular canal as the predilective point for penetration of the labyrinth capsule in suppurative middle-ear disease, regards as the best clinical test the alternate rarefaction and condensation of air in the middle ear by means of the Siegle otoscope, or the rarefactor of Delstanche, firmly inserted into the external auditory canal. The indicative symptoms are usually wanting in children under one year of age, and in patients with an intact vestibular apparatus; the nystagmus, during compression, is directed toward the diseased, and during rarefaction toward the sound side. In cases of chronic suppurative middle-ear disease with positive fistula symptoms and absence of hearing, labyrinth infection may be assumed and operative interference regarded as indicated.

The Influence of Cold Bathing and Swimming upon the Ear and its Diseases.—The establishment of swimming as a part of the customary education of males, in Japan, and the large number of swimming schools, both inland and upon the sea coast, afforded the inducement, as well as the opportunity, for the observations of DR. SHIN, IZI ZIBA (*Arch. f. Ohrenheilk.*, November, 1911). These were made through the medium of the aural clinic of the University of Tokio, when special hearing tests seemed necessary, and were commenced a few days before the usual date for the opening of the swimming schools, which are usually in operation for three months in the year. The material observed consisted of 1916 male individuals ranging from the age of six to thirty years, pupils of the 16 fresh-water and 7 salt-water swimming schools in Tokio. Of this total, the first examination gave 642 individuals with abnormalities detailed in the following list: Cerumen, 469; chronic suppurative middle-ear disease, 61; furunculosis of the external canal, 11; perforation of the drumhead, 40; cicatricial closure of previous perforations, 57; hyperemia of the drumhead, 4; 33.5 per cent. of the whole number examined. The number of cases with ceruminous accumulation was large, as compared with average clinical reports, 73 per cent., the preponderating number being in young children, but in none of these cases was the accumulation occlusive, a fact in accord with the observations of Politzer and Bezold. Next in number came the existent and past cases of suppurative middle-ear disease; the cases in which hyperemia of the drumhead was observed gave no evidence of middle-ear implication. One month after the first observation a second examination of the same material was made, with the resultant addition of 164 patients, 8.5 per cent., to the list,

classified as follows: Cerumen, 330; chronic suppurative middle-ear disease, 61; furunculosis, 302; recurrence of suppurative middle-ear disease, 17; acute middle-ear disease with perforation of the drumhead, 3; open perforation of the drumhead, 29; perforation of the drumhead, cicatricially closed, 51; hyperemia of the drumhead, 10; subjective noises in the ear, 3; in all, 806 cases, 42 per cent. of the total material. The decrease in the number of cases of ceruminous accumulation was apparently due to the effect of water entering the external auditory canal and softening the accumulated mass, or else causing it to swell and occlude the canal, causing impairment of hearing and the application of measures for relief. The increase in the number of cases of furunculosis is especially interesting in the light of the conclusions drawn by Dr. Shin, who refers the frequency of this malady not only to the entrance of water into the external canal and the subsequent irritative and infective efforts at its removal, but also to the favoring influence of exposure to the heat of the sun. It is a matter of common observation in Japan that furunculosis of the ear is more frequent in the sea-beach than in the river swimming schools, 55.1 per cent. of cases in the former, and 41.87 per cent. in the latter, a difference by no means entirely imputable to the more irritative effect of the salt water, since, in the pauses between swims the beach bathers are exposed freely to the rays of the sun, while the river bathers are sheltered by barracks. As a supporting evidence is the fact that 60 per cent. of the cases of furunculosis affected the left ear, the remaining 40 per cent. being right-sided or binaural. In middle Japan right-sided swimming is the preferential exercise, the left side of the body and head being most exposed to the sun; moreover, a further investigation of the swimming habit of the patients with furunculosis of the right ear showed that the majority of them swam upon the left side. It was further found that this frequent malady was much less common among the cases with ceruminous accumulation and much less painful, when it did occur, in consequence probably both of the protection afforded by the accumulated mass and its remedial effect when moistened and swollen. In the cases of subjective noises this symptom was found to be due to a general circulatory rather than to an aural cause, and the hyperemia of the drumhead was usually the result of too prolonged or too forcible local efforts to remove water remaining at the inner end of the canal after the bath. In the comparison drawn between the first and second examination of the cases of chronic suppurative middle-ear disease, Dr. Shin observed no case of deleterious result; the majority of the cases exhibited much greater cleanliness, if not material improvement, as the result of the daily bathing. The recurrent suppurative inflammations of the middle ear were, in all instances, subacute, with an injected drumhead and a mucous or seropurulent discharge, and there were 3 cases of acute perforative middle-ear inflammation in patients whose ears were intact at the first examination; in all of these cases there was furunculosis, and in one of them the injection of the drumhead and the acute middle-ear congestion, with ultimate perforation of the drumhead and a seropurulent discharge, followed the furunculosis. In reference to the question of the frequency of middle-ear implication in swimming by entrance of water through the tympanopharyngeal tube, Dr. Shin is of the opinion that

this does not occur except under unusual causative conditions, entailing considerable variation in air pressure in the nasopharynx, especially sneezing and blowing the nose. As a test in this matter three pupils, with dry persistent drumhead perforations, had the affected ears tightly stopped with plugs of cotton and lard, and then dove five times successively from a springboard, four meters above the water, the middle ears remaining dry. In conclusion Dr. Shin lays stress upon the importance of preliminary and successive aural examinations in all swimming-school pupils, and advises even those with sound ears to use some measure of protection from the possibility of a furuncular infection.

HYGIENE AND PUBLIC HEALTH

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The Purification of Water by Anhydrous Chlorine.—C. R. DARNELL (*Jour. Amer. Pub. Health Assoc.*, November, 1911, i, 783) states that anhydrous chlorine possesses considerable advantages over the hypochlorites, which have been used rather extensively for the purification of water during the last few years. Ordinarily chlorine is introduced into water as hypochlorite of lime. Although the hypochlorite treatment of water has been successful, there are certain disadvantages attending the use of hypochlorites for this purpose. The hypochlorites are unstable compounds and the content of available chlorine is rather uncertain, necessitating frequent chemical examinations in order to determine the quantity to be used. Another objection in the use of hypochlorites is the fact that more or less troublesome dosing devices must be used. It has also been noticed that a relatively slight excess of hypochlorites may impart a disagreeable taste and unpleasant odor to the water. Chlorine is obtained in considerable quantities, at the present time, as a by-product in the manufacture of caustic soda. This chlorine is purified, dried, liquefied by pressure, and placed on the market in steel drums or cylinders. Chlorine so obtained is practically chemically pure, containing merely traces of oxygen, carbon dioxide, and nitrogen. It is necessary in marketing chlorine in this form to remove all water vapor in order to prevent corrosion of the steel used in the construction of the storage drums. The price of this liquefied chlorine varies from ten to fifteen cents per pound. Water at ordinary temperature will absorb about 4000 parts per million, by weight, of chlorine. It will be readily seen that this property of chlorine is of considerable importance in water purification, since it makes it unnecessary to use elaborate mixing devices which would be the case were the

chlorine not so easily soluble. In general it may be stated that an average unfiltered river water will require about one-half of a part, by weight of chlorine gas per million parts of water, to bring about a satisfactory bacterial purification. In other words, it will require from three to four pounds of liquefied chlorine per million gallons of water. Darnell has invented a relatively simple automatic apparatus for the introduction and mixing of chlorine gas with water. This apparatus occupies but a small space, and, judging from the results obtained by its use, is efficient. The important advantages which this method of applying dry chlorine gas has over the use of hypochlorites may be summarized briefly as follows: For cities already having aqueducts and the necessary water supply it is possible to disinfect large amounts of water in a plant occupying little space. A mixing chamber 16 inches in diameter and 24 feet long, for example, has a capacity of 750,000 gallons per day. To purify the water of greater New York, 750,000,000 gallons per day, 16 mixing chambers 10 feet in diameter and 200 feet long would be sufficient. This would occupy about one acre of ground. The cost of labor for operating such a plant would be trifling. The cost of the chlorine would range, roughly speaking, from 35 to 50 cents per million gallons of water. In comparing this with other purification methods Darnell points out that anhydrous chlorine and ozone have practically the same efficiency. The chlorine method, however, is cheaper to operate and rather more reliable because there is no complicated electrical machinery necessary. It also requires less labor. When we compare chlorine and hypochlorites, we find that the advantage of chlorine over hypochlorites consists first in the uniform composition of chlorine, contrasting, in a noteworthy manner, with the variability of the hypochlorites; second in the relatively small amount of apparatus which is required for adding chlorine to the water supply. Finally, in contrasting chlorine and filtration, it may be noted that a chlorine purifying plant is cheaper to install than a filter plant, and it is cheaper to operate because the labor required is much less. It should be stated that in the chlorine method provision must be made for clarifying the water before the chlorine is added, so that it will usually be necessary to have preliminary sedimenting reservoirs or mechanical filters, for the chlorine in no way clarifies a turbid water.

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All communications should be addressed to—

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JOHN A. HARTWELL, M.D., Assistant Professor of Surgery and Professor of Clinical Surgery in the Cornell University Medical College, New York.

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HOWARD FOX, M.D., Assistant Visiting Dermatologist to the German Hospital, New York.

Sarcoma of the Tongue and Allied Conditions.
EDWARD MILTON FOOTE, M.D., Adjunct Professor of Surgery in the New York Polyclinic.

The Differential Diagnosis of Cerebral Hemorrhage and Thrombosis.
CHARLES W. BURR, M.D., Professor of Mental Diseases in the University of Pennsylvania, Philadelphia.

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HERBERT C. MOFFITT, M.D., Professor of the Principles and Practice of Medicine in the University of California, San Francisco, Cal.

Reactions Induced by Antityphoid Vaccination.
HENRY ALBERT, M.D., Professor of Pathology and Bacteriology in the University of Iowa, and A. M. MENDENHALL, M.D., Instructor in Pathology and Bacteriology in the University of Iowa, Iowa City, Iowa.

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CHARLES D. AARON, M.D., Professor of Gastro-enterology and Adjunct Professor of Dietetics in Detroit College of Medicine.

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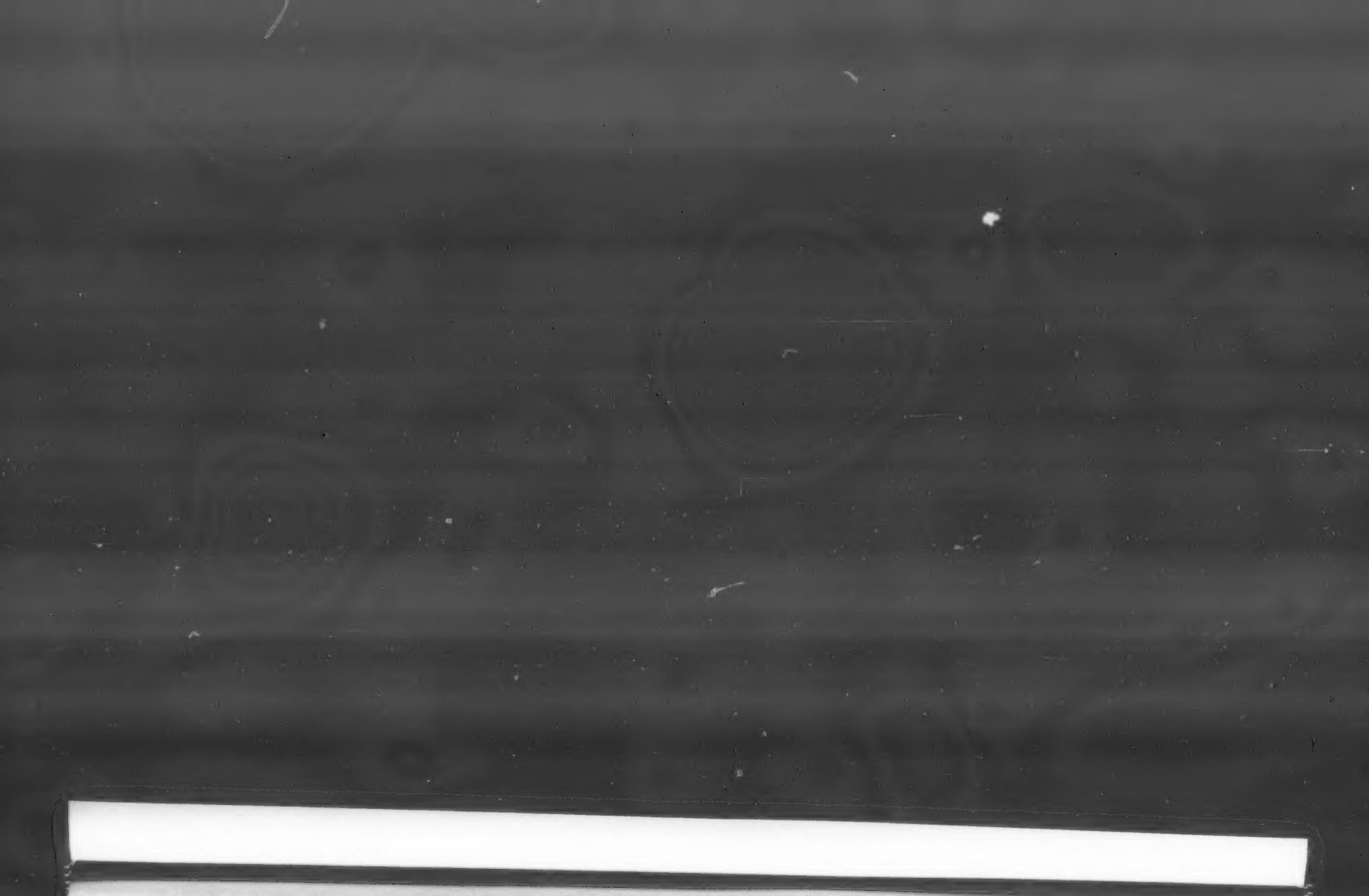

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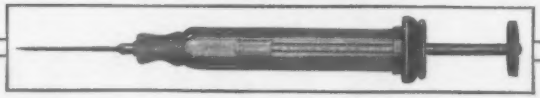

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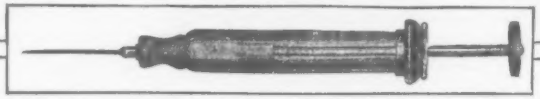

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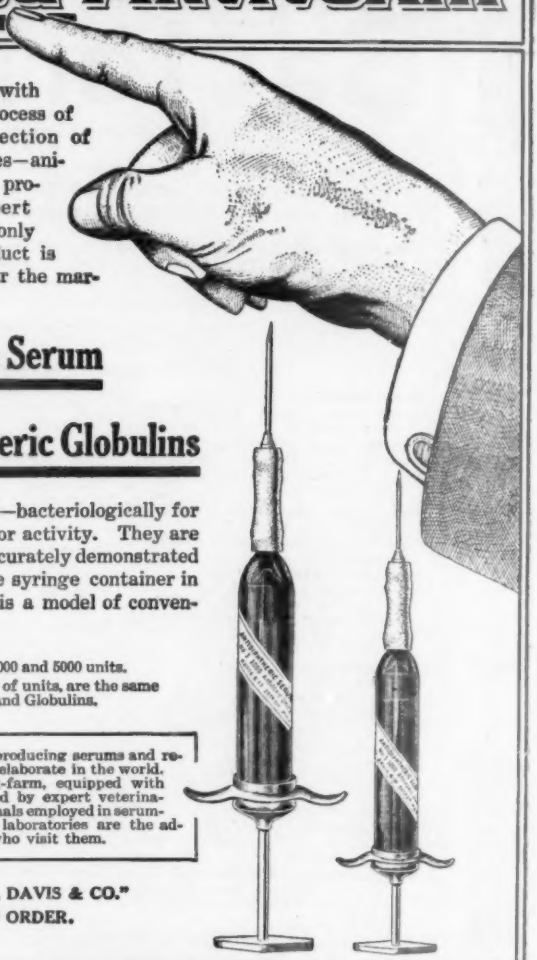

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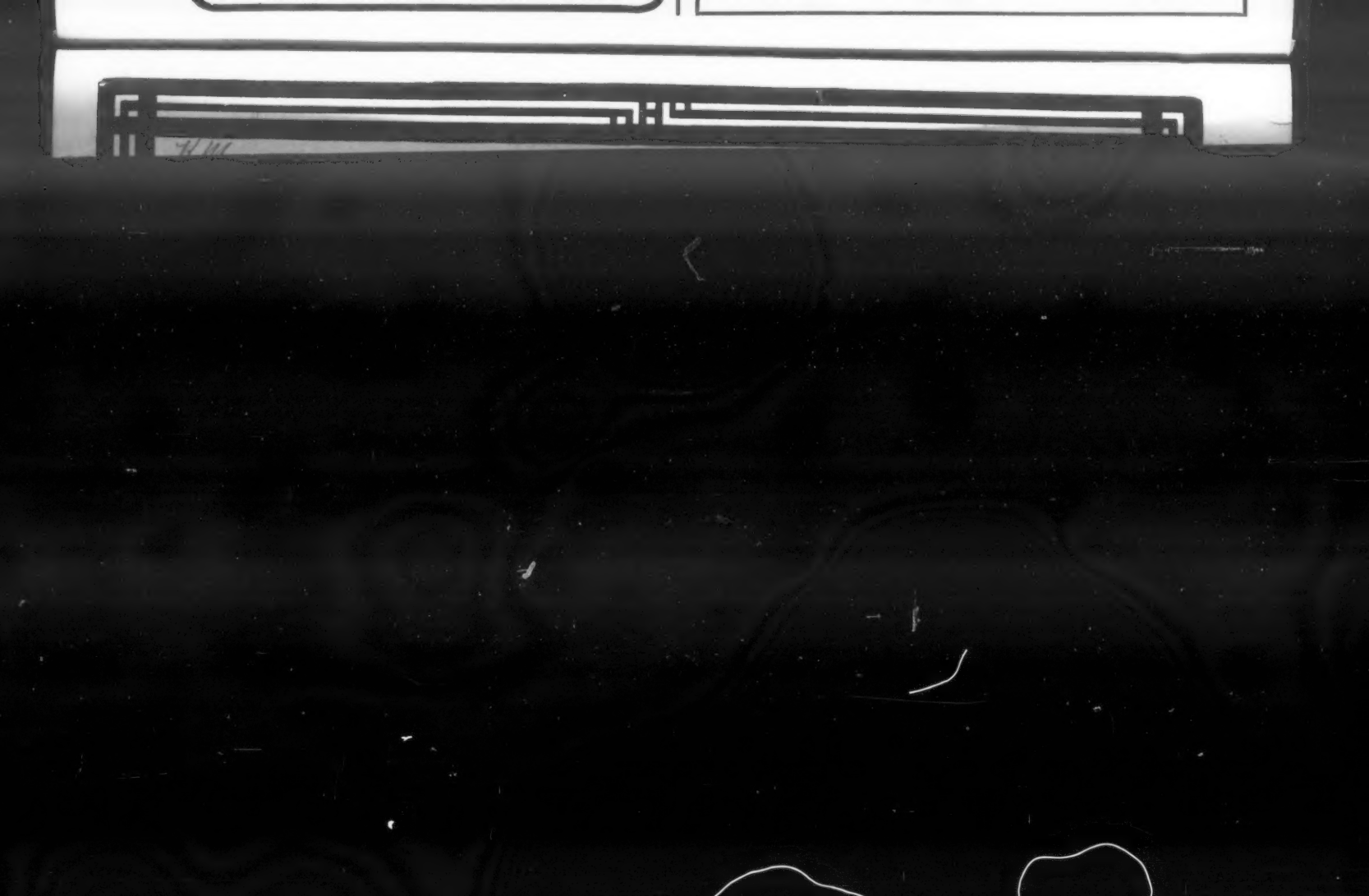

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